* * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * * *

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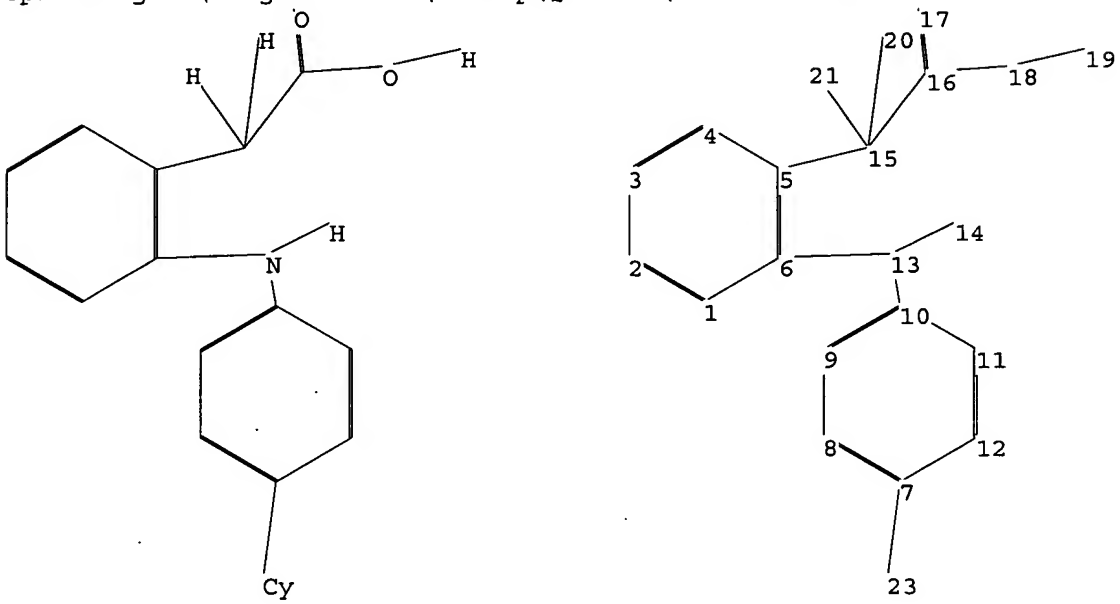
Uploading C:\Program Files\Stnexp\Queries\10724457.str



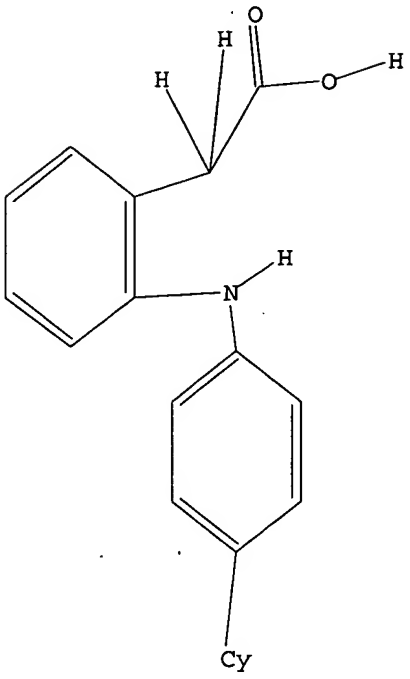
chain nodes :
13 14 15 16 17 18 19 20 21 23
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12
chain bonds :
5-15 6-13 7-23 10-13 13-14 15-16 15-20 15-21 16-17 16-18 18-19
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12
exact/norm bonds :
6-13 7-23 10-13
exact bonds :
5-15 13-14 15-16 15-20 15-21 18-19
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 16-17 16-18
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS 21:CLASS 23:Atom

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 full
L3 141 SEA SSS FUL L1

=> file ca

=> s l3
L4 1 L3

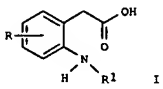
=> d ibib abs fhitstr

L4 ANSWER 1 OF 1 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 141:38434 CA
TITLE: Preparation of substituted amino phenylacetic acids and derivatives and their use as cyclooxygenase-2 (COX-2) inhibitors
INVENTOR(S): Fujimoto, Roger Aki; McQuire, Leslie Wighton; Monovich, Lauren G.; Mugrage, Benjamin Biro; Parker, David Thomas; Van Duzer, John Henry; Wattanasin, Sompong
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004048314	A1	20040610	WO 2003-EP13246	20031125
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SY, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2507458	AA	20040610	CA 2003-2507458	20031125
US 2004132769	A1	20040708	US 2003-724457	20031125
EP 1567477	A1	20050831	EP 2003-767652	20031125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: US 2002-429222P P 20021126
WO 2003-EP13246 W 20031125

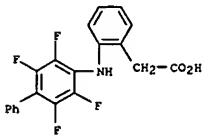
OTHER SOURCE(S): MARPAT 141:38434
GI



I

AB The title compds. I (R = H, alkyl, cycloalkyl, halo, alkoxy, F3CO, Me3C, cyano, R1 = biaryl, β-naphthyl derivative, bicyclic heterocyclic aryl, cycloalkyl monocyclic carbocyclic aryl, cycloalkane fused-monocyclic carbocyclic aryl) were prepared Thus, N,N-dimethyl-2-(2',3',5',6'-tetrafluoro-4'-phenylanilino)phenylacetamide was hydrolyzed to give I (R =

L4 ANSWER 1 OF 1 CA COPYRIGHT 2005 ACS on STN (Continued)
H, R1 = 4-PhC6F4).
IT 702641-10-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (aminophenyl)acetic acid derivs. and their cyclooxygenase-2
inhibitory activity for treating rheumatoid arthritis, osteoarthritis, pain, dysmenorrhea, neoplasms, and inflammation)
RN 702641-10-9 CA
CN Benzeneacetic acid, 2-[(2,3,5,6-tetrafluoro[1,1'-biphenyl]-4-yl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> file marpat

=> s l1 full
L5            60 SEA SSS FUL L1

=> s l5/com
L6            59 L5/COM

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```

L6 ANSWER 1 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 142:463449 MARPAT
TITLE: Preparation of biphenylsulfonic acid derivatives as EDG receptor antagonists for treatment of inflammation
INVENTOR(S): Sato, Shin; Nakamura, Takeshi; Nara, Futoshi; Komesu, Kiyoaki
PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 193 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2005120047	A2	20050512	JP 2003-358892	20031020

PRIORITY APPLN. INFO.: JP 2003-358892 20031020
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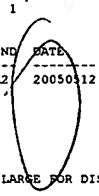
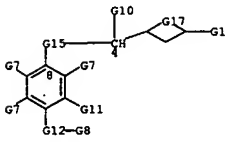


* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. I [wherein R1 = H or (un)substituted alkyl; R2 = H, OH, CO2H, etc.; R3 = H, OH, aralkyloxy, etc.; X = alkylamino, OH, amino, or alkoxy; Y = CO2H, SO3H, or PO3H; Z = O, S, CO, etc.; ring A = (un)substituted (hetero)cyclyl; ring B = (un)substituted cyclyl] or salts or esters thereof are prepared as endothelial differentiation gene (EDG) receptor antagonists for the treatment of inflammatory disease. For example, the compound II•Na was prepared in a multi-step synthesis in good yield. II•Na inhibited EDG-1 with IC50 of 0.018 μM. I are useful for the treatment of inflammation, cerebral ischemia, spasm, etc. (no data).

MSTR 1



G3 = CO2H
G8 = Ph (opt. substd. by 1 or more G9)
G9 = alkyl <containing 1-6 C>

L6 ANSWER 1 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
(opt. substd. by 1 or more G3)
G12 = NH
G13 = R <"4-7 member ring forming group", containing zero or more N, zero or more O, zero or more S, 1 or more double bonds>
G15 = 6-8 5-4

Patent location: claim 1
Note: or salts and esters

L6 ANSWER 2 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 142:355039 MARPAT
TITLE: Preparation of substituted aryloximes as inhibitors of PAI-1
INVENTOR(S): Havran, Lisa Marie; Butera, John Anthony; Elokdah, Hassan Mahmoud; Jenkins, Douglas John; Gundersen, Eric Gould
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: U.S. Pat. Appl. Publ., 32 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005070584	A1	20050331	US 2004-948611	20040923
WO 2005030193	A1	20050407	WO 2004-US31460	20040924
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW		
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG		

PRIORITY APPLN. INFO.: US 2003-505801P 20030925
US 2004-948611 20040923
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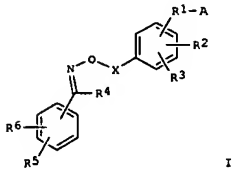
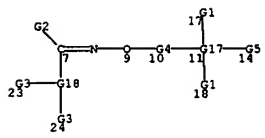


I

AB Title compds. I [R1 = bond, alkylene, etc.; R2-3 = H, halo, alkyl, etc.; R4 = H, (cyclo)alkyl; A = carboxy or acid mimic; X = (cyclo)alkylene, alkoxy; R5-6 = H, halo, alkyl, etc.] are prepared For instance, [4-[3-[[[1-(4-tert-butylphenyl)ethylidene]amino]oxy]propoxy]phenyl]acetic acid (II) is prepared from Me 4-hydroxyphenylacetic acid, 1,3-dibromopropane and 1-(4-tert-butylphenyl)ethanone oxime. At 25 μM, II exhibited 39% inhibition of PAI-1. I are useful for the treatment of, e.g.,

L6 ANSWER 2 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)

MSTR 1



G8 = 208

G9 = NH
G11 = alkylene <containing 1-4 C> (opt. substd.)
G12 = CO2H
G17 = 73-10 68-14 69-17 70-18

G19 = Ph
Patent location: claim 1
Note: or pharmaceutically acceptable salts or esters

L6 ANSWER 3 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 142:254663 MARPAT
TITLE: Amine-containing phenyl derivative melanin-concentrating hormone receptor antagonists for therapeutic use
INVENTOR(S): Tempest, Paul; Hulme, Christopher; Ma, Vu
PATENT ASSIGNEE(S): Amgen, Inc., USA
SOURCE: PCT Int. Appl., 319 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005019240	A2	20050303	WO 2004-US25970	20040811
WO 2005019240	A3	20050506		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-494855P 20030813
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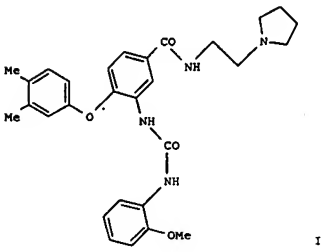
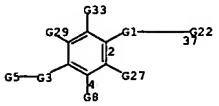


I

L6 ANSWER 3 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
AB The title compds., or pharmaceutically-acceptable salts, tautomers or prodrugs thereof, are provided. Also provided are methods for treating or preventing a melanin-concentrating hormone-mediated disorder in a subject, comprising administering to a subject in need of such treatment or prevention a compound of the invention. Preparation of compds, e.g. I, is described.

MSTR 1



G9 = NH
G10 = Ph (opt. substd. by G37)
G27 = alkyl (opt. substd. by 1 or more G28)
G28 = CO2H
G37 = Ph
Patent location: claim 1
Note: or pharmaceutically acceptable salts, tautomers, or prodrugs
Note: additional substitution also claimed

L6 ANSWER 4 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 142:219050 MARPAT
TITLE: Preparation of arylcarboxylates as antibacterials.
INVENTOR(S): Leslie, Bruce W.; Lawson, Christopher; Woolley, Christopher; Zhao, Lihua; Thomas, Michael; Grant, Richard; Thomson, Samantha
PATENT ASSIGNEE(S): Pantherix Ltd, UK
SOURCE: Brit. UK Pat. Appl., 39 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2404855	A1	20050216	GB 2003-15878	20030707

PRIORITY APPLN. INFO.: GB 2003-15878 20030707
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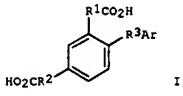
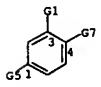


I

AB A compound for therapeutic use comprises a title compound [I; R1-R3 = Yn; Y = CH2, CH:CH, CO, O, NH, S, SO, SO2; n = 0-2; Ar = (fused) (aromatic) carbocyclyl, heterocyclyl which may contain any degree of saturation or contain a CO group, and is optionally substituted by Me OH, OMe, CO2H, CONH2, SO2NH2, SO2Me, SOMe, SMe, CF3, Ph, heterocyclyl, etc.; ≥1 of the terminal CO2H groups may be replaced by a polar group] (no synthetic or biol. data).

MSTR 1



G3 = (1-2) CH2
G4 = CO2H
G8 = NH
G9 = Ph (opt. substd. by 1 or more G18)
G18 = pyrazolyl
Patent location: claim 1

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

L6 ANSWER 4 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)

L6 ANSWER 5 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 142:176543 MARPAT
TITLE: Preparation of arylalkyne derivatives having EDG receptor antagonist effect
INVENTOR(S): Sato, Susumu; Nakamura, Takeshi; Nara, Futoshi; Komesu, Kiyoaki
PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 181 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2005022986	A2	20050127	JP 2003-187530	20030630

PRIORITY APPLN. INFO.: JP 2003-187530 20030630
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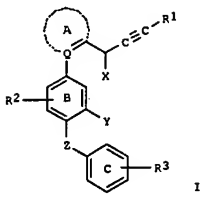


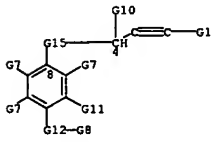
I

AB The title compds. (I), or salts or esters thereof [R1 = (un)substituted C1-17 alkyl optionally containing 1 or ≥2 of a double or triple bond, (un)substituted benzene ring, O, S, SO, SO2, and (un)substituted NH; R2 represents 1-3 substituents selected from H, HO, CO2H, NO2, halo, alkoxy, alkenyloxy, alkynyloxy, aralkyloxy, NH2, alkylamino, alkanoylamino, alkylthio, and (un)substituted C1-6 alkyl; R3 represents 1-3 substituents selected from H, HO, aralkyloxy, alkylamino, alkanoylamino, alkylthio, CO2H, NO2, halo, and (un)substituted C1-10 alkyl; X = alkylamino, HO, NH2, (un)substituted C1-6 alkoxy; Y = CO2H, SO3H, P(O)(OH)2; Z = O, S, (un)substituted NH, CO, SO, SO2, (un)substituted CH2; ring A = (un)substituted 4- to 7-membered ring containing -Q:C- as a partial structure and optionally containing 1 or ≥2 of CH:CH, N, O, (un)substituted NH, S, and CO; Q = C, N] are prepared These compds. are endothelial differentiation gene 1 (EDG-1) receptor antagonists and effective in preventing and/or treating inflammations, diseases associated with abnormal

L6 ANSWER 5 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
Note: or salts and esters

L6 ANSWER 5 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
angiogenesis, cerebral vascular spasm, brain ischemia, cancer-related diseases, cerebral infarction, myocardial infarction, nephritis, pneumonia, immune diseases, Crohn's disease, colitis, or chronic diarrhea.
Thus, Suzuki coupling of Me 5-bromo-2-[(4-butoxyphenyl)thio]benzoate with 2-formylphenylboronic acid in the presence of tetrakis(triphenylphosphine)palladium in a mixt. of 4.6 M aq. K2CO3 soln. in 1,2-dimethoxyethane at 60° for 5 h to give 99% Me 4-[(4-butoxyphenyl)thio]-2'-formyl-1,1'-biphenyl-3-carboxylate (II). 2-[[7-(2-Propynyloxy)heptyl]oxy]tetrahydro-2H-pyran was treated with 1.6 M BuLi/hexane in THF at -78°, stirred for 10 min, treated dropwise with a soln. of II in THF, and stirred for 1 h to give 78% Me 4-[(4-butoxyphenyl)thio]-2'-[1-hydroxy-4-[[7-[(tetrahydro-2H-pyran-2-yl)oxy]heptyl]oxy]-2-butynyl]-1,1'-biphenyl-3-carboxylate which was stirred in the presence of pyridinium p-toluenesulfonate in ethanol at 60° for 1 h to give 82% Me 4-[(4-butoxyphenyl)thio]-2'-[1-hydroxy-4-[(7-hydroxyheptyl)oxy]-2-butynyl]-1,1'-biphenyl-3-carboxylate (III). III was heated with NaOH in aq. dioxane at 90° for 8 h to give 76% sodium 4-[(4-butoxyphenyl)thio]-2'-[1-hydroxy-4-[(7-hydroxyheptyl)oxy]-2-butynyl]-1,1'-biphenyl-3-carboxylate (IV). IV inhibited the sphingosine-1-phosphate-stimulated prodn. of cAMP in CHO cells expressing Edg-1 with IC50 of 0.020 μM.

MSTR 1



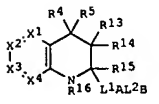
G3 = CO2H
G8 = Ph (opt. substd. by 1 or more G9)
G9 = alkyl <containing 1-6 C> (opt. substd. by 1 or more G3)
G12 = NH
G13 = R <"4-7 member ring forming group", containing zero or more N, zero or more O, zero or more S, 1 or more double bonds>
G15 = 6-8 5-4

Patent location: claim 1

L6 ANSWER 6 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 141:295874 MARPAT
TITLE: Preparation of tetrahydroquinoline derivatives as inhibitors of serine protease enzymes of the coagulation cascade and/or contact activation system.
INVENTOR(S): Quan, Mimi L.; Wang, Cailan; Zhou, Jinglan; Hangeland, Jon J.; Seiffert, Dietmar A.; Knabb, Robert M.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 150 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004080971	A1	20040923	WO 2004-US7216	20040310
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004235847	A1	20041125	US 2004-796396	20040309

PRIORITY APPLN. INFO.: US 2003-453812P 20030311
US 2004-796396 20040309
GI

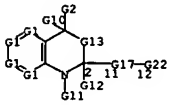


I

AB Title compds. [I; L1 = bond, CH2, CH2CH2, CH2O, CH2CO, etc.; L2 = bond, O, CO, CO2, S, SO, SO2, CONR8, SO2NR8, etc.; A = (substituted) carbocyclylene, heterocyclylene; B = (substituted) alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl; X1-X4 = CR1, CR2, N, etc.; R1 = H, F, Cl, Br, iodo, OCF3, CF3, cyano, NH2, alkylamino, dialkylamino, CONH2, CH2CH2NH2, etc.; R2 = H, F, Cl, Br, iodo, OCF3, CF3, cyano, NO2, amino, aminocarbonyl, (substituted) alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, etc.; R4 = H, F, haloalkyl, (substituted) alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, etc.; R5 = H, F, haloalkyl, (substituted) alkyl, alkenyl, alkynyl, heterocyclyl(alkyl), etc.; R13 = H, F, alkyl, aminoalkyl, CF3, aminocarbonyl, etc.; R14 = H, alkyl,

L6 ANSWER 6 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
aminoalkyl, F, CF3, aminocarbonyl, etc.; R13R14 = O; R15 = H, alkyl; R16 =
H, alkyl, PhCH2, alkylcarbonyl, alkylsulfonyl, alkoxycarbonyl], were prepd. Thus, 4-amidinobenzamidine monohydrochloride, styrene, 1'-formyl-1-benzyloxycarbonyl-4-isobutylcarbamoylbiphenyl (prepn. given) and indium triflate were heated together at 70° in MeCN for 12 h to give a product which was hydrogenolyzed in MeOH/HOAc over Pd/C to give 2'-(6-carbamimidoyl-4-phenyl-1,2,3,4-tetrahydroquinolin-2-yl)-4-isobutylcarbamoylbiphenyl-2-carboxylic acid. I inhibited Factor XIa with Ki ≤15 μM.

MSTR 1



G1 = 106

G13 = 41

G17 = p-C6H4 (opt. substd. by 1 or more G39)
G23 = NH (opt. substd.)
G29 = Ph (opt. substd. by 1 or more G32)
G32 = CH2CO2H
Patent location: claim 1
Note: substitution is restricted
Note: or pharmaceutically acceptable salts or hydrates
Note: additional ring formation and substitution also claimed
Stereochemistry: or stereoisomers

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

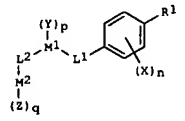
L6 ANSWER 7 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 141:295728 MARPAT
TITLE: Preparation of benzene derivatives as cannabinoid receptor ligands
INVENTOR(S): Shankar, Bandarpalle B.; Rizvi, Razia K.; Kozlowski, Joseph A.; Shih, Neng-Yang
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 53 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004186148	A1	20040923	US 2004-803577	20040318
WO 2004085385	A2	20041007	WO 2004-US8333	20040318
WO 2004085385	A3	20041125		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-456268P 20030320
GI

L6 ANSWER 7 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)



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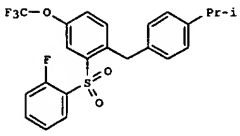
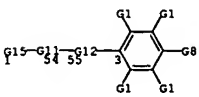


II

AB Compds. of the formula I [R1 = H, alkoxy, alkyl, aryl, etc.; X = H, alkoxy, cycloalkyl, aryl, etc.; Y = H, OH, CN, alkoxy, alkyl, etc.; Z = H, OH, CN, halo, alkoxy, etc.; L1 = bond, -CF2-, carbonyl, O, S, etc.; L2 = bond, carbonyl, S, SO, SO2, etc.; M1 = aryl cycloalkyl, heteroaryl, heterocycloalkyl; M2 = alkyl, aryl, cycloalkyl, heteroaryl, etc.; n = 0-4; p = 0-4; q = 0-5; with provisions] and the pharmaceutically acceptable salt or solvates thereof, are prepared and disclosed as possessing anti-inflammatory and immunomodulatory activity. Thus, e.g., II was prepared via addition of 4-isopropylphenyllithium (in situ generation from the aryl bromide) to 2-(2-fluorobenzyl)-4-trifluorobenzaldehyde, with subsequent reductive dehydroxylation and sulfur dioxidn. In cannabinoid receptor assays, I demonstrated Ki values ranging from 0.1 nM to 1000 nM. Also disclosed are pharmaceutical compns. containing said compds.

MSTR 1A



G8 = cyclopropyl
G11 = 148-1 147-55

L6 ANSWER 7 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)

G12 = NH
G18 = CH2
G19 = CO2H
Patent location: claim 1
Note: or pharmaceutically acceptable salts or solvates
Note: additional substitution also claimed
Note: additional ring formation also claimed

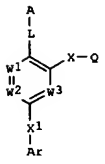
L6 ANSWER 8 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 141:225166 MARPAT
TITLE: Preparation of benzylnaphthalenes for the treatment of viral infection
INVENTOR(S): Ernst, Justin T.; Boman, Erik; Ceide, Susana C.; Montalban, Antonio G.; Nakanishi, Hiroshi; Roberts, Edward; Saiah, Eddine; Lum, Christopher
PATENT ASSIGNEE(S): Kemia Inc., USA
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004071426	A2	20040826	WO 2004-US3411	20040206
WO 2004071426	A3	20050324		

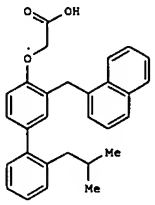
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004248850	A1	20041209	US 2004-774040	20040206
PRIORITY APPLN. INFO.:			US 2003-446713P	20030211
			US 2003-523217P	20031118

OTHER SOURCE(S): CASREACT 141:225166
GI



I

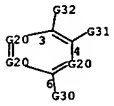


II

L6 ANSWER 8 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)

AB Title compds. I [wherein A = H, OH, NO2, CO2R, CONROH, COCF3, B(OH)2, SO3H, PO3R2, OPO3R2, CONHSO2R, (un)substituted heterocyclyl; L, X = independently (un)substituted (CH2)m, O(CH2)m, SOO-2(CH2)m, NR(CH2)m, NRCO(CH2)m, CO2(CH2)m, CONR(CH2)m, NRCO2(CH2)m, NRCONR(CH2)m, SO2NR(CH2)m, NRSO2(CH2)m; W1 = N, CR1; W2 = N, CR2, W3 = N, CR3; X1 = a bond, O, SOO-2, NR, NCOR, NCO2R, NCONR2, NRCO, NRCONR, (un)substituted alkyl, alkenyl, acetylenyl; Q = (un)substituted cycloalkyl, cycloalkenyl, aryl(alkyl), heterocyclyl(alkyl); Ar = (un)substituted aryl, heterocyclyl; R = independently H, (un)substituted alkyl, alkenyl, alkynyl, alkylenearyl, alkyleneheterocyclyl; R1-R3 = independently H, halo, CN, NO2, (un)substituted alkyl, alkenyl, alkylenearyl, alkyleneheterocyclyl, alkoxy, acyl, carboxy, amino, carbamoyl, ureido, sulfamoyl, etc.; m = 0-4; and stereoisomers, tautomers, solvates, prodrugs, and pharmaceutically acceptable salts thereof] were prepared For example, coupling of 1-bromonaphthalene with 4-bromoanisaldehyde gave 1-(5-bromo-2-methoxybenzyl)naphthalene (88%), which was substituted with tert-Bu bromoacetate to afford the 4-bromophenoxyacetate (96%). Palladium catalyzed reaction with bis(pinacolato)diboron (75%), followed by reaction with 2-isobutylphenyl trifluoromethanesulfonate in the presence of Pd(PPh3)4 and hydrolysis of the ester with TFA provided II (34%). I and their pharmaceutical compns. are expected to be useful for the treatment of viral infection, particularly HIV infection (no data).

MSTR 1



G1 = CO2H
G15 = (1-4) CH2
G20 = CH (opt. substd.)
G21 = NH (opt. substd.)
G22 = 100

$p\text{-}C_6H_4Ph_{100}$

Patent location: claim 2
Note: substitution is restricted
Note: and tautomers, solvates, prodrugs, and pharmaceutically acceptable salts

L6 ANSWER 8 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
Note: also incorporates claims 73, 77, 81 and 83
Stereochemistry: and stereoisomers

L6 ANSWER 9 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 141:71442 MARPAT
TITLE: Preparation of aryl, aryloxy, and alkyloxy substituted 1H-indol-3-yl glyoxylic acid derivatives as inhibitors of plasminogen activator inhibitor-1 (PAI-1)
INVENTOR(S): Jennings, Lee Dalton; Elokdah, Hassan Mahmoud; McFarlane, Geraldine Ruth
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004052854	A2	20040624	WO 2003-US38934	20031209
WO 2004052854	A3	20040805		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004138283	A1	20040715	US 2003-731308	20031209
PRIORITY APPLN. INFO.:			US 2002-432329P	20021210

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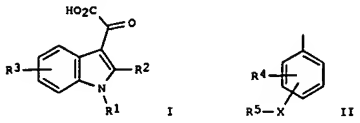
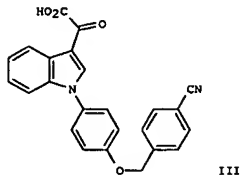
L6 ANSWER 9 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)



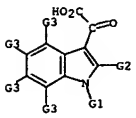
I II



III

AB The title compds. [I; R1 = II (wherein R4 = H, halo, alkyl, etc.; X = O, S, NH; R5 = alkyl, perfluoroalkyl, cycloalkyl, etc.), alkyl, benzo[1,3]dioxol-5-ylmethyl, cycloalkylalkyl, etc.; R2 = H, alkyl, cycloalkyl, etc.; R3 = H, halo, alkyl, etc.], useful as inhibitors of plasminogen activator inhibitor (PAI-1) for treating conditions resulting from fibrinolytic disorders, such as deep vein thrombosis, coronary heart disease and pulmonary fibrosis, were prepared E.g., a 4-step synthesis of
III, starting from indole and 4-iodoanisole, which showed 23% PAI-1 inhibition at 25 μM, was given. The pharmaceutical composition comprising
the compound I is claimed.

MSTR 1



G3 = Ph (opt. substd. by 1 or more G25)
G6 = Ph (opt. substd. by 1 or more G26)

L6 ANSWER 9 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
G9 = NH
G26 = CH2CO2H
Patent location: claim 1
Note: or pharmaceutically acceptable salts or esters

L6 ANSWER 10 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 141:38434 MARPAT
TITLE: Preparation of substituted amino phenylacetic acids and derivatives and their use as cyclooxygenase-2 (COX-2) inhibitors
INVENTOR(S): Fujimoto, Roger Aki; McQuire, Leslie Wighton; Monovich, Lauren G.; Mugrage, Benjamin Biro; Parker, David Thomas; Van Duzer, John Henry; Wattanasin, Sompong
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004048314	A1	20040610	WO 2003-EP13246	20031125
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SY, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2507458	AA	20040610	CA 2003-2507458	20031125
US 2004132769	A1	20040708	US 2003-724457	20031125
EP 1567477	A1	20050831	EP 2003-767652	20031125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: US 2002-429222P 20021126
WO 2003-EP13246 20031125

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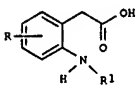
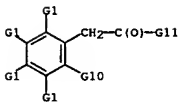


I

AB The title compds. I (R = H, alkyl, cycloalkyl, halo, alkoxy, F3CO, Me3C, cyano, R1 = biaryl, β-naphthyl derivative, bicyclic heterocyclic aryl, cycloalkyl monocyclic carbocyclic aryl, cycloalkane fused-monocyclic carbocyclic aryl) were prepared Thus, N,N-dimethyl-2-(2',3',5',6'-tetrafluoro-4'-phenylanilino)phenylacetamide was hydrolyzed to give I (R = H, R1 = 4-PhC6F4).

MSTR 1

L6 ANSWER 10 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)



G10 = 9

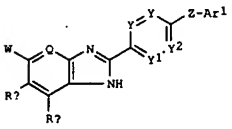
G11 = OH
G16 = phenylene (opt. substd.)
G17 = cyclopropyl
Patent location: claim 1
Note: or pharmaceutically acceptable salts or esters
Note: also incorporates claim 13

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 138:338144 MARPAT
TITLE: Preparation of 2-phenyl benzimidazoles and imidazo-[4,5]pyridines as Cds1/Chk2-inhibitors and adjuvants to chemotherapy or radiation therapy in the treatment of cancer
INVENTOR(S): Arienti, Kristen L.; Axe, Frank U.; Breitenbucher, J. Guy; Huang, Liming; Lee, Alice; McClure, Kelly J.
PATENT ASSIGNEE(S): Ortho-McNeil Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 144 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

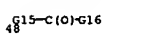
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003032984	A1	20030424	WO 2002-US33371	20021018
WO 2003032984	C1	20031120		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2464000	AA	20030424	CA 2002-2464000	20021018
US 2003176438	A1	20030918	US 2002-273487	20021018
EP 1435947	A1	20040714	EP 2002-770620	20021018
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002006161	A	20050201	BR 2002-6161	20021018
JP 2005506349	T2	20050303	JP 2003-535787	20021018
NO 2003002759	A	20030818	NO 2003-2759	20030617
ZA 2003005533	A	20041018	ZA 2003-5533	20030717
PRIORITY APPLN. INFO.:			US 2001-330304P	20011019
			WO 2002-US33371	20021018

GI



I

L6 ANSWER 11 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)



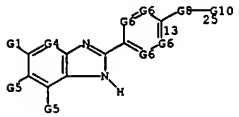
G15 = alkylene <containing 1-6 C>
G16 = OH
Patent location: claim 1
Note: and pharmaceutically acceptable salts, esters or amides
Stereochemistry: and enantiomers, diastereomers

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)

AB 2-Aryl-substituted benzimidazoles and imidazo[4,5]pyridines (shown as I; e.g. 2-[4-(4-chlorophenoxy)phenyl]-1H-benzimidazole-5-carboxylic acid amide (II)) are disclosed as inhibitors of Cds1 and useful as adjuvants to chemotherapy or radiation therapy in the treatment of cancer. For I: W is COOH, -C(O)NHR1, or -SO2NHR1 (R1 is H or C1-4alkyl); Q is N or CH; Ra and Rb are H or halogen; Y, Y1 and Y2 = N and C-Rc with the proviso that 0, 1 or 2 of Y, Y1 and Y2 are N and at least 2 of Rc must be H; Rc = -H, -OH, -C1-6alkyl, -SCF3, halo, -CF3 and -OCF3; Z = O, S, SO, SO2, SO2NR2, NR2SO2, NH, CONR2, piperazinediyl or a covalent bond; R2 is H or C1-4alkyl; Ar1 is an aromatic group as defined in the claims. IC50 values are reported for inhibition of human Cds1 checkpoint kinase by 103 examples of I, e.g. 3 nM for 2-[4-(4-chloro-3-trifluoromethylphenoxy)phenyl]-1H-benzimidazole-5-carboxylic acid amide. Addnl. studies were (i) determination of the effect of II on tumor cell line clonogenic survival, (ii) effect of II on tumor growth in murine xenograft models, (iii) determination of the effect of 14 examples of I on radiation-induced apoptosis in isolated primary cells, and (iv) determination of the effect of II on radiation-induced apoptosis in splenocytes in vivo. Although the methods of preparation are not claimed, .apprx.100 example prepns. are included.

MSTR 1



G4 = N
G6 = 23

G8 = NH
G10 = Ph (opt. substd. by (1-3) G11)
G11 = 48

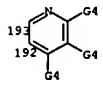
L6 ANSWER 12 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 138:238024 MARPAT
TITLE: Aryl substituted pyridines as blockers of sodium channels
INVENTOR(S): Shao, Bin; Goehring, R. Richard; Victory, Samuel F.; Sun, Qun
PATENT ASSIGNEE(S): Euro-Celtique S.A., USA
SOURCE: U.S. Pat. Appl. Publ., 27 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003055088	A1	20030320	US 2002-235673	20020906
PRIORITY APPLN. INFO.:			US 2001-317526P	20010907

AB Title aryl substituted pyridines as blockers of sodium channels, for the treatment of neuronal damage following global and focal ischemia, for the treatment or prevention of neurodegenerative conditions such as amyotrophic lateral sclerosis (ALS), and for the treatment, prevention or amelioration of both acute or chronic pain, as antitinnitus agents, as anticonvulsants, and as antimanic depressants, as local anesthetics, as antiarrhythmics and for the treatment or prevention of diabetic neuropathy, have a structure ArR1R2R3R4C6N wherein C6N is a pyridine ring, Ar and R1-R4 are set in the specification. Thus, 2-[4-(4-fluorophenoxy)phenyl]pyridine 5-carboxylic acid 2-(N-piperidinyl)ethylamide was prepared from reaction of 2-chloropyridine 5-carboxylic acid 2-(N-piperidinyl)ethylamide 563 mg and 4-(4-fluorophenoxy)phenyl boronic acid 557 mg at 85° in the presence of Pd(Ph3)4, and the evaluationof the sodium channel blocker property after an electrophysiol. in vitro assay was 0.95 Ki/μM.

MSTR 1

G2 = 193-3 192-187



G5 = p-C6H4 (opt. substd. by (1-2) G18)
G7 = NH
G18 = alkyl (substd. by CO2H)
G20 = Ph (opt. substd. by 1 or more G18)
Patent location: claim 1
Note: or pharmaceutically acceptable salts, prodrugs, solvates, or radiolabels
Note: additional substitution also claimed

L6 ANSWER 12 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
Note: substitution is restricted

L6 ANSWER 13 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 138:238022 MARPAT
TITLE: Preparation of substituted 2-(4-phenoxyphenyl)pyridine derivatives and related compounds as sodium channel blockers for the treatment of neuronal damage and neurodegenerative conditions
INVENTOR(S): Shao, Bin; Goehring, R. Richard
PATENT ASSIGNEE(S): Euro-Celtique S.A., Luxembourg
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003022285	A1	20030320	WO 2002-US28299	20020906
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2459531	AA	20030320	CA 2002-2459531	20020906
US 2003073724	A1	20030417	US 2002-235670	20020906
US 6770661	B2	20040803		
EP 1432424	A1	20040630	EP 2002-770470	20020906
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002012327	A	20040921	BR 2002-12327	20020906
JP 2005501916	T2	20050120	JP 2003-526414	20020906

PRIORITY APPLN. INFO.: US 2001-317455P 20010907
WO 2002-US28299 20020906

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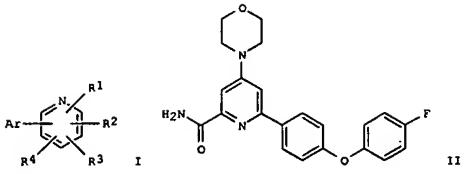
L6 ANSWER 13 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)



I II

AB Title compds. I [wherein Ar = (un)substituted C6H4-p-XPh, naphthyl, or C6H4-p-XR9; R1 = (un)substituted alkyl, amino, alkylthiol, COR10, SO2R10, or OCONH2; R2 = Ym(CH2)nZ; R3 and R4 = independently H, halo, OH, CN, NH2, (di)alkylamino, alkoxy, or (un)substituted (cyclo)alkyl, alkenyl, alkynyl, or carbamoyl; R9 = (un)substituted alkyl; R10 = (un)substituted alkyl, alkenyl, alkynyl, OR12, NH2, (di)alkylamino, alkenylamino, dialkylaminoalkenyl, dialkylaminoalkylamino, hydroxyaminoalkenylamino, (hetero)cycloalkyl, aryl(alkyl), etc.; R11 = H or alkyl; R12 = H, (un)substituted alkyl, or alkali metal; X = absent, O, S, NH, or CH2; Y = O, S, or NR11; Z = (un)substituted saturated heterocyclic ring; m = 0 or 1; n = 0-6; with provisos; or pharmaceutically acceptable salts, prodrugs, or solvates thereof] were prepared as sodium channel blockers. For example, cyclization of 4-(phenylamino)-3-penten-2-one with 4-(4-fluorophenoxy)benzonitrile in the presence of 2,2,6,6-tetramethylpiperidine in THF provided 2-methyl-6-[4-(4-fluorophenoxy)phenyl]-4-pyridinone. Chlorination with POCl3 in the presence of DBU in CH2Cl2, coupling with morpholine in the presence of NaH, oxidation of the Me group to the carboxylic acid using SeO2 in pyridine, esterification with MeOH and SOCl2, and conversion to the amide with NH3 in MeOH gave II. In an electrophysiol. in vitro assay, the latter showed activity as a sodium channel blocker with Ki of 0.29 μM. Thus, I are useful for the treatment of neuronal damage following global and focal ischemia, neurodegenerative conditions such as amyotrophic lateral sclerosis (ALS), and acute or chronic pain, including diabetic neuropathy (no data). In addition, I may be used as anti-tinnitus agents, anticonvulsants, anti-manic depressants, local anesthetics, and antiarrhythmics (no data).

MSTR 1

G3—G2

G2 = pyridyl (substd. by G28)
G5 = p-C6H4 (opt. substd. by (1-2) G18)
G7 = NH
G18 = alkyl (substd. by CO2H)
G20 = Ph (opt. substd. by 1 or more G18)

L6 ANSWER 13 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
Patent location: claim 1
Note: or pharmaceutically acceptable salts, prodrugs, solvates, or radiolabels
Note: additional substitution also claimed
Note: substitution is restricted

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L6 ANSWER 14 OF 59 MARPAT COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 138:238021 MARPAT
TITLE: Preparation of aryl-substituted pyridinecarboxamides as sodium channel blockers for treatment of neuronal damage and neurodegenerative conditions
INVENTOR(S): Shao, Bin; Goehring, R. Richard; Victory, Samuel F.; Sun, Qun
PATENT ASSIGNEE(S): Euro-Celtique S.A., Luxembourg
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003022276	A1	20030320	WO 2002-US28298	20020906
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2459527	AA	20030320	CA 2002-2459527	20020906
EP 1432419	A1	20040630	EP 2002-773292	20020906
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002012338	A	20040921	BR 2002-12338	20020906
JP 2005506981	T2	20050310	JP 2003-526405	20020906
PRIORITY APPLN. INFO.:			US 2001-317526P	20010907
			WO 2002-US28298	20020906

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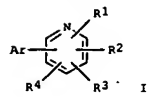
L6 ANSWER 14 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)



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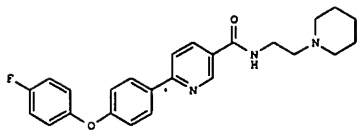


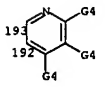
II

AB Title compds. I (wherein Ar = (un)substituted C6H4-p-XPh, naphthyl, or C6H4-p-XR9; R1 = (un)substituted alkyl, amino, alkylthiol, COR10, SO2R10, or OCONH2; R2 = Ym(CH2)nZ; R3 and R4 = independently H, halo, OH, CN, NH2, (di)alkylamino, alkoxy, or (un)substituted (cyclo)alkyl, alkenyl, alkynyl, or carbamoyl; R9 = (un)substituted alkyl; R10 = (un)substituted alkyl, alkenyl, alkynyl, OR12, NH2, (di)alkylamino, alkenylamino, dialkylaminoalkenyl, dialkylaminoalkylamino, hydroxyaminoalkenylamino, (hetero)cycloalkyl, aryl(alkyl), etc.; R11 = H or alkyl; R12 = H, (un)substituted alkyl, or alkali metal; X = absent, O, S, NH, or CH2; Y = O, S, or NR11; Z = (un)substituted saturated heterocyclic ring; m = 0 or 1; n = 0-6; with provisos; or pharmaceutically acceptable salts, prodrugs, or solvates thereof) were prepared as sodium channel blockers. For example, condensation of 6-chloronicotinic acid with 1-(2-aminoethyl)piperidine in the presence of HOBT and DIC in DMF gave the carboxamide (no data). Coupling with 4-(4-fluorophenoxy)phenylboronic acid in the presence of Pd(PPh3)4 and K2CO3 in DME and H2O provided II. In an electrophysiol. in vitro assay, the latter showed activity as a sodium channel blocker with Ki of 0.95 μM. Thus, I are useful for the treatment of neuronal damage following global and focal ischemia, neurodegenerative conditions such as amyotrophic lateral sclerosis (ALS), and acute or chronic pain, including diabetic neuropathy (no data). In addition, I may be used as anti-tinnitus agents, anticonvulsants, anti-manic depressants, local anesthetics, and antiarrhythmics (no data).

MSTR 1

L6 ANSWER 14 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)

G2 = 193-3 192-187



G5 = p-C6H4 (opt. substd. by (1-2) G18)
G7 = NH
G18 = alkyl (substd. by CO2H)
G20 = Ph (opt. substd. by 1 or more G18)
Patent location: claim 1
Note: or pharmaceutically acceptable salts, prodrugs, solvates, or radiolabels
Note: additional substitution also claimed
Note: substitution is restricted

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 15 OF 59 MARPAT COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 136:380081 MARPAT
TITLE: Urea derivative malaria parasite anion channel blockers for treating malaria
INVENTOR(S): Christophersen, Palle; Dahl, Bjarne H.
PATENT ASSIGNEE(S): Neurosearch A/S, Den.
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002039987	A2	20020523	WO 2001-DK745	20011112
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002023492	A5	20020527	AU 2002-23492	20011112
PRIORITY APPLN. INFO.:			DK 2000-1705	20001114
			US 2000-252467P	20001122
			WO 2001-DK745	20011112

AB The present invention relates to the use of malaria anion channel blockers for treating malaria, a method for screening the activity of a compound in the above use, a method for diagnosing the severity of malaria disease of a subject, and novel compds. active as anion channel blockers. One example compound prepared was N-2,3-difluorophenyl-N'-3-trifluoromethylphenylthiourea.

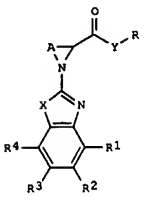
MSTR 1

G1 = Ph (opt. substd. by 1 or more G27)
G16 = phenylene (opt. substd. by 1 or more G28)
G17 = CH2CO2H
G19 = NH
G27 = Ph
Patent location: claim 1
Note: or pharmaceutically acceptable salts or prodrugs

L6 ANSWER 16 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 136:309922 MARPAT
TITLE: Preparation of benzoxazolyl piperidines and analogs as rotamase enzyme inhibitors
INVENTOR(S): Kemp, Mark Ian; Palmer, Michael John; Sanner, Mark Allen; Wythes, Martin James
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S., 43 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6372736	B1	20020416	US 1999-358107	19990721
US 6562964	B1	20030513	US 2002-56901	20020123
PRIORITY APPLN. INFO.:			GB 1998-15880	19980721
			US 1999-358107	19990721

GI



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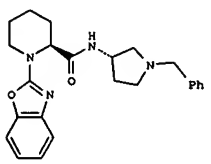
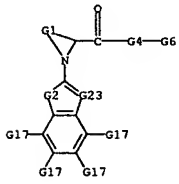


II

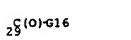
AB Title compds. [I; A = (un)substituted unbranched C3-C5 alkylene; X and Y = independently O, S, NH, or N-alkyl; R = (un)substituted, C-linked, 4- to 6-membered, non-aromatic, heterocyclic ring containing 1 N; R1-R4 = independently H, halo, (cyclo)alkyl, haloalkyl, (cyclo)alkoxy, CONR5R6, cycloalkylalkylene, cycloalkylalkoxy, or CO2R7; R5 and R6 = independently H, alkyl, or taken together = unbranched alkylene; R7 = alkyl] were prepared as rotamase enzyme inhibitors, particularly FKBP-12 and FKBP-52 inhibitors. Thus, (2S)-1-(1,3-benzoxazol-2-yl)-2-piperidinecarboxylic acid (preparation given) was amidated with (3S)-1-benzylpyrrolidine-3-ylamine in the presence of 1-hydroxybenzotriazole hydrate and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide.HCl in CH2Cl2 to yield II.

L6 ANSWER 16 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
Twenty-one compds. of the invention demonstrated inhibitory activity against human recombinant FKBP-12 in a coupled colorimetric PPIase in vitro assay with IC50 values below 1200 nM, and II inhibited the rotamase enzyme FKBP-52 in a similar assay with IC50 = 2790 nM. As neurotrophic agents, the invention compds. promote neuronal regeneration and outgrowth and are useful for the treatment of neurodegenerative diseases or other disorders involving nerve damage.

MSTR 1



G7 = alkyl <containing 1-6 C> (opt. substd. by (1-2) G12)
G8 = alkylamino <containing 1-6 C> / azetidino
G12 = Ph (opt. substd. by (1-3) G8) / 29



Patent location: claim 1

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 17 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 136:232111 MARPAT
TITLE: Process for making N-arylanthranilic acids and their derivatives
INVENTOR(S): Chen, Michael Huai Gu; Davis, Edward Mark; Magano, Javier; Nanninga, Thomas Norman; Winkle, Derick Dale
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

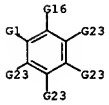
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002018319	A1	20020307	WO 2001-US22948	20010720
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2420003	AA	20020307	CA 2001-2420003	20010720
AU 2001077044	A5	20020313	AU 2001-77044	20010720
EP 1313694	A1	20030528	EP 2001-954824	20010720
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001013520	A	20030624	BR 2001-13520	20010720
JP 2004507518	T2	20040311	JP 2002-523437	20010720
US 2004039208	A1	20040226	US 2003-344294	20030207
ZA 2003001182	A	20040512	ZA 2003-1182	20030212
NO 2003000844	A	20030225	NO 2003-844	20030224
BG 107635	A	20040930	BG 2003-107635	20030313
PRIORITY APPLN. INFO.:			US 2000-228206P	20000825
			WO 2001-US22948	20010720

OTHER SOURCE(S): CASREACT 136:232111

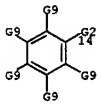
AB N-arylanthranilic acids, their esters, amides, and hydroxamic esters are prepared by coupling 1 equivalent of an aniline derivative with 1 equivalent of an aromatic carboxylic acid carrying a leaving group, such as halo, alkyl- or arylsulfonyloxy, or phosphate, in presence of .apprx. 10 equivalent base. Thus, 2,3,4-F3C6H2CO2H was coupled with 2,4-Cl(I)C6H3NH2 in presence of LiN(CHMe2)2 in THF. The base was added at intervals at -20° with warming to room temp between addns. and the yield of 3,4-F2C6H3NHC6H3(I)Cl-4,2 was 78%. This compound was converted to the acid chloride and treated with cyclopropylmethoxyamine hydrochloride to give the N-cyclopropylmethoxyamide. The process is suitable for industrial production

MSTR 1

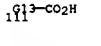
L6 ANSWER 17 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)



G1 = 14



G2 = NH
G9 = Ph (opt. substd.)
G13 = (1-4) CH2
G23 = 111



Patent location: claim 1
Note: additional substitution and fused ring formation also claimed
Note: or pharmaceutically acceptable salts
Note: substitution is restricted
Note: also incorporates claim 76, formula Ij

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

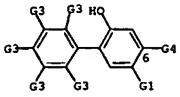
L6 ANSWER 18 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:352783 MARPAT
TITLE: Methods for inhibiting proliferation and inducing apoptosis in cancer cells
INVENTOR(S): Adrian, Thomas E.
PATENT ASSIGNEE(S): Creighton University, USA
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085166	A1	20011115	WO 2001-US40697	20010508
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2408622	AA	20011115	CA 2001-2408622	20010508
BR 2001010473	A	20030401	BR 2001-10473	20010508
EP 1326605	A1	20030716	EP 2001-935770	20010508
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NZ 522387	A	20030926	NZ 2001-522387	20010508
JP 2003532675	T2	20031105	JP 2001-581820	20010508
NO 2002005343	A	20030109	NO 2002-5343	20021107
US 2004053962	A1	20040318	US 2003-275590	20030602
PRIORITY APPLN. INFO.:			US 2000-219344P	20000509
			WO 2001-US40697	20010508

AB Disclosed are methods of decreasing proliferation of adenocarcinoma cancer cells, or of inducing apoptosis of adenocarcinoma cancer cells, or of inducing differentiation of adenocarcinoma cancer cells into non-cancerous cells. One such method includes contacting the adenocarcinoma cancer cells with a compound under conditions effective for the compound to inhibit binding of leukotriene B4 to leukotriene B4 receptor. In another such method, the method includes contacting the adenocarcinoma cancer cells with 2-(2-propyl-3-(3-(2-ethyl-4-(4-fluorophenyl)-5-hydroxyphenoxy)propoxy)phenoxy)benzoic acid or a pharmaceutically acceptable salt, solvate, or congener thereof. Also disclosed are methods of treating adenocarcinomas in a subject. One method includes administering to the subject an amount of a compound effective to inhibit binding of leukotriene B4 to leukotriene B4 receptor. Another method includes administering 2-(2-propyl-3-(3-(2-ethyl-4-(4-fluorophenyl)-5-hydroxyphenoxy)propoxy)phenoxy)benzoic acid or a pharmaceutically acceptable salt, solvate, or congener thereof, to the subject.

L6 ANSWER 18 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)

MSTR 1



G17 = OH
G27 = 144-20 145-96 148-131

G29 = 206

G30 = carbon chain <containing 1-8 C>
G35 = 223

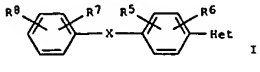
G41 = phenylene (opt. substd. by (1) halo)
G42 = NH
Patent location: claim 5
Note: substitution is restricted
Note: or pharmaceutically acceptable salts or solvates

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 19 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:272968 MARPAT
TITLE: Preparation of aryl-substituted pyrazoles, triazoles, and tetrazoles and their anticonvulsant and sodium channel blocking properties
INVENTOR(S): Hogenkamp, Derk; Nguyen, Phong; Yang, Ji
PATENT ASSIGNEE(S): Cocensys, Inc., USA
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001072714	A2	20011004	WO 2001-US8972	20010322
WO 2001072714	A3	20020530		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2400778	AA	20011004	CA 2001-2400778	20010322
US 2002006947	A1	20020117	US 2001-814123	20010322
BR 2001008819	A	20021210	BR 2001-8819	20010322
EP 1292577	A2	20030319	EP 2001-918874	20010322
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003528859	T2	20030930	JP 2001-570627	20010322
NZ 520875	A	20050429	NZ 2001-520875	20010322
ZA 2002006534	A	20030815	ZA 2002-6534	20020815
NO 2002004426	A	20020916	NO 2002-4426	20020916
US 2004002523	A1	20040101	US 2003-456735	20030609
US 6919363	B2	20050719		
PRIORITY APPLN. INFO.:			US 2000-191757P	20000324
			US 2001-814123	20010322
			WO 2001-US8972	20010322

GI

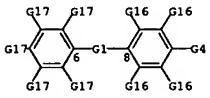


I

AB The title compds. I [Het = N heteroaryl; R5-R8 = H, halo, haloalkyl, alkyl, amino, ureido, etc.; X = O, S, NR9, CH2, NR9CO, CONR9 and R9 = H, alkyl] were prepared The invention also is directed to the use of I for the treatment of neuronal damage following global and focal ischemia, for the treatment or prevention of neurodegenerative conditions such as amyotrophic lateral sclerosis (ALS), and for the treatment, prevention or amelioration of both acute or chronic pain, as antitinnitus agents, as

L6 ANSWER 19 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
anticonvulsants, and as antimanic depressants, as local anesthetics, as antiarrhythmics and for the treatment or prevention of diabetic neuropathy. E.g., reaction of 1-fluoro-4-nitrobenzene with 4-{[1,2,4]triazol-1-yl}phenol gave 37% 1-[4-(4-nitrophenoxy)phenyl]-1H-[1,2,4]triazole.

MSTR 1



G1 = NH
G4 = 25

G17 = alkyl (substd. by CO2H)
Patent location: claim 1
Note: substitution is restricted
Note: or pharmaceutically acceptable salts, prodrugs, or solvates

L6 ANSWER 20 OF 59 MARPAT COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 135:257270 MARPAT
TITLE: Preparation of aryl substituted pyridines, pyrimidines, pyrazines and triazines with anticonvulsant and sodium channel blocking activity
INVENTOR(S): Hogenkamp, Derk J.; Nguyen, Phong; Shao, Bin
PATENT ASSIGNEE(S): Cocensys, Inc., USA
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068612	A2	20010920	WO 2001-US7797	20010312
WO 2001068612	A3	20020314		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2400945	AA	20010920	CA 2001-2400945	20010312
US 2002040025	A1	20020404	US 2001-803659	20010312
US 6867210	B2	20050315		
EP 1265866	A2	20021218	EP 2001-918558	20010312
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003527376	T2	20030916	JP 2001-567706	20010312
BR 2001008918	A	20040629	BR 2001-8918	20010312
NZ 521866	A	20050324	NZ 2001-521866	20010312
ZA 2002007069	A	20031203	ZA 2002-7069	20020903
NO 2002004308	A	20021108	NO 2002-4308	20020909
US 2004192691	A1	20040930	US 2003-738989	20031219
US 2005043305	A1	20050224	US 2004-951861	20040929

PRIORITY APPLN. INFO.: US 2000-188188P 20000310
US 2001-803659 20010312
WO 2001-US7797 20010312

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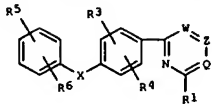
L6 ANSWER 20 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)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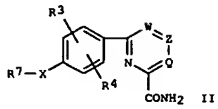
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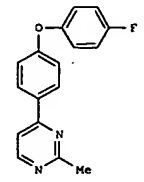
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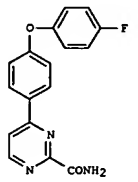
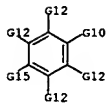

IV

AB The title aryl substituted heterocyclic compds. I and II [Q, Z, W = CR2, N; R1 = alkyl, H2N, alkylthio, R8CO, R8SO2, H2NCO2, 2-imidazolinyl, 3-pyrazolyl, etc; R2 = H, (un)substituted alkyl, alkenyl alkynyl, halo, HO, cycloalkyl, cyano, H2N, alkoxy, alkylaminocarbonyl; R1R2 together form heterocycle; R3, R4, R5, R6 = H, alkyl, alkenyl, halo, HO, NO2, H2N, cyano, H2NCO, ureido, azido, alkoxy, CO2H, etc; R7 = (un)substituted alkyl; R8 = alkyl, alkenyl, R9O, H2N, substituted H2N, cycloalkyl; R9 = H, alkyl, alkali metal; X = O, S, NH, CH2] and their pharmaceutically acceptable salts, prodrugs, or solvates were prepared and were useful for the treatment of neuronal damage following ischemia, the treatment of amyotrophic lateral sclerosis, the treatment of acute or chronic pain, as antitinnitus agents, as anticonvulsants, as antimanic depressants, as local anesthetics, as antiarrhythmics, and for the treatment of diabetic neuropathy. Thus, K2CO3 induced substitution reaction of 4-FC6H4OH with 4-FC6H4COMe gave 80% 1-[4-(4-fluorophenoxy)phenyl]ethanone which underwent successive condensation with DMF di-Me acetal and cyclocondensation with acetamidine HCl to give the [(fluorophenoxy)phenyl]pyrimidine III. Selenium dioxide oxidation of III and subsequent amidation with carbonyl diimidazole/NH4OAc in DMF gave the pyrimidinecarboxamide IV which blocked electroshock-induced seizures in mice with ED50 of 0.7 mg/kg i.v. IV also possessed sodium channel blocking activity with an apparent antagonist dissociation constant for inactivated sodium channels of 0.49μM.

MSTR 1

L6 ANSWER 20 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)



G1 = N
G10 = 2

G16 = NH
G17 = Ph (opt. substd. by (1-2) G18)
G18 = alkyl (substd. by CO2H)
Patent location: claim 1
Note: or pharmaceutically acceptable salts, prodrugs or solvates
Note: substitution is restricted

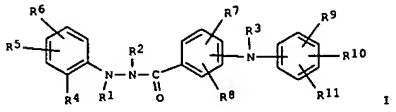
L6 ANSWER 21 OF 59 MARPAT COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 135:137306 MARPAT
TITLE: Preparation of N-arylhydrazide compounds as remedies for dementia
INVENTOR(S): Shinkai, Hisashi; Ozeki, Hidekazu; Kosugi, Yoshinori
PATENT ASSIGNEE(S): Japan Tobacco Inc., Japan
SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001055093	A1	20010802	WO 2001-JP393	20010122
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
JP 2002145840	A2	20020522	JP 2001-15192	20010124

PRIORITY APPLN. INFO.: JP 2000-16157 20000125
JP 2000-264744 20000901

GI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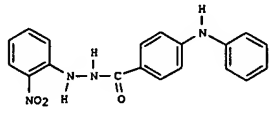
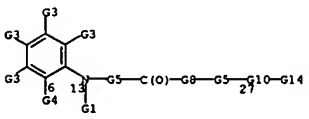

II

AB The title compds. I [R1, R2, R3 = H, alkyl; or R1R4 = (CH2)2, etc.; R4, R5, R6 = H, alkoxy, etc.; R7, R8 = H, arylalkyl, etc.; R9, R11 = H, nitro, etc.; R10 = H, etc.] are prepared I exhibit inhibitory activity against the aggregation of β-amyloid and show antioxidant activity; I are useful as preventive and therapeutic agents for dementia, particularly

L6 ANSWER 21 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
Alzheimer-type dementia. The title compd. II in vitro showed IC50 of 0.36
μM against the aggregation of β-amyloid. A formulation is given.

MSTR 1



G5 = NH
G8 = phenylene (opt. substd. by (up to 2) G9)
G9 = alkyl <containing 1-6 C> (substd. by 1 or more G10)
G10 = phenylene (opt. substd. by (up to 2) G11)
G11 = Ph
G18 = CO2H
Derivative: or pharmaceutically acceptable salts
Patent location: claim 1
Note: substitution is restricted

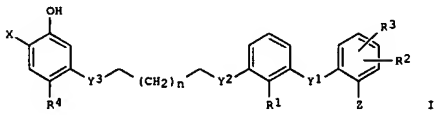
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L6 ANSWER 22 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 134:366682 MARPAT
TITLE: Oncolytic combinations for the treatment of cancer
INVENTOR(S): Sawyer, Jason Scott; Teicher, Beverly Ann; Beight, Douglas Wade; Smith, Edward C. R.; McMillen, William Thomas
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 270 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034198	A2	20010517	WO 2000-US30941	20001109
WO 2001034198	A3	20020214		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-164900P 19991111
GI



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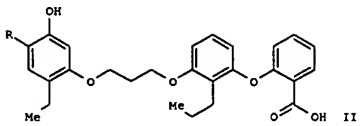
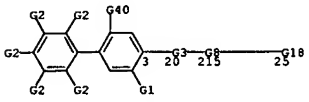


II

AB A method of treating cancer that comprises administering a patient ionizing radiation in conjunction with effective amts. of a

L6 ANSWER 22 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
2',2'-difluoronucleoside anti-cancer compd. and a leukotriene LTB4 inhibitor (I) [wherein X = a 5-membered (un)substituted heterocycle or fused bicyclic radical consisting of a carbocyclic group fused to 2 adjacent C atoms of a 5-membered (un)substituted heterocycle; Y1 = a bond or divalent linking group contg. 1-9 atoms; Y2 and Y3 = independently CH2, O, or S; Z = an acidic group; R1 = (alk)aryl, cycloalkyl, (ar)alkyl, (ar)alkenyl, alkynyl, haloalkyl, aryloxy, or alkoxy; R2 = H, halo(alkyl), alkoxy, (cyclo)alkyl, acidic group, or (CH2)1-7-acidic group; R3 = (cyclo)alkyl, (CH2)1-7-cycloalkyl, alkenyl, alkynyl, benzyl, or aryl; n = 0-6] is disclosed. Examples includes 17 syntheses, 22 formulations, and Lewis lung test results. For instance, benzylation of 1-[2-hydroxy-4-(3-chloropropoxy)-5-ethylphenyl]ethanone (69%), coupling the ethanone with 2-(3-hydroxy-2-propylphenoxy)benzoic acid Me ester (72%), oxidn. to give the α-hydroxy ketone (31%), cyclization with triflic anhydride and formamide to give the oxazole (6%), debenzylation with BF3•OEt2 (45%), and deesterification (92%) afforded II (R = 4-oxazolyl). Treatment of C57B1 mice with 100 mg/kg of the LTB4 antagonist, 2-[2-propyl-3-[3-[2-ethyl-5-hydroxy-4-(4-fluorophenyl)phenoxy]propoxy]phenoxy]benzoic acid (II; R = 4-FC6H4), 60 mg/kg of gemcitabine•HCl, and 400 Rads of radiation delayed growth of murine Lewis lung carcinoma by an av. of 32.3 days, compared to a delay of 13.4 days using the gemcitabine•HCl and radiation combination. In addn., the mean no. of lung metastases was reduced from 11.5 to 7.0.

MSTR 3



G10 = carbon chain <containing 1-8 C>
G11 = 37

G12 = OH
G23 = NH
G24 = phenylene (opt. substd. by (1) G25)
G31 = 168

G32 = phenylene (substd. by (1) G9)
Patent location: claim 13

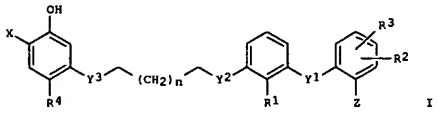
L6 ANSWER 22 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
Note: substitution is restricted

L6 ANSWER 23 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 134:366681 MARPAT
TITLE: Oncolytic combinations for the treatment of cancer
INVENTOR(S): Sawyer, Jason Scott; Teicher, Beverly Ann; Beight, Douglas Wade; Smith, Edward C. R.; McMillen, William Thomas
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 250 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034197	A2	20010517	WO 2000-US30839	20001109
WO 2001034197	A3	20020510		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-164704P 19991111
GI



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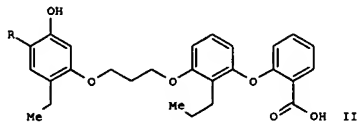
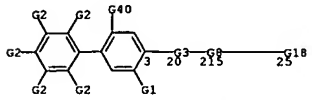


II

AB A method of treating cancer with radiation in conjunction with the administration of a leukotriene LTB4 inhibitor (I) [wherein X = a

L6 ANSWER 23 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
5-membered (un)substituted heterocycle or fused bicyclic radical consisting of a carbocyclic group fused to 2 adjacent C atoms of a 5-membered (un)substituted heterocycle; Y1 = a bond or divalent linking group contg. 1-9 atoms; Y2 and Y3 = independently CH2, O, or S; Z = an acidic group; R1 = (alk)aryl, cycloalkyl, (ar)alkyl, (ar)alkenyl, alkynyl, haloalkyl, aryloxy, or alkoxy; R2 = H, halo(alkyl), alkoxy, (cyclo)alkyl, acidic group, or (CH2)1-7-acidic group; R3 = (cyclo)alkyl, (CH2)1-7-cycloalkyl, alkenyl, alkynyl, benzyl, or aryl; n = 0-6] is disclosed. Examples includes 17 syntheses, 7 formulations, nude mouse xenograft test results, and Lewis lung test results. For instance, benzylation of 1-[2-hydroxy-4-(3-chloropropoxy)-5-ethylphenyl]ethanone (69%), coupling the ethanone with 2-(3-hydroxy-2-propylphenoxy)benzoic acid Me ester (72%), oxidn. to give the α-hydroxy ketone (31%), cyclization with triflic anhydride and formamide to give the oxazole (6%), debenzylation with BF3•OEt2 (45%), and deesterification (92%) afforded II (R = 4-oxazolyl). Treatment of mice with 100 mg/kg of the LTB4 antagonist, 2-[2-propyl-3-[3-[2-ethyl-5-hydroxy-4-(4-fluorophenyl)phenoxy]propoxy]phenoxy]benzoic acid (II; R = 4-FC6H4) and 400 Rads of radiation delayed growth of human DU145 prostate carcinoma by an av. of 31.5 days, compared to a delay of 19.2 days using radiation alone. In the Lewis lung test, the mean no. of lung metastases was reduced from 15.5 using radiation alone to 12.0 using the combination therapy.

MSTR 2



G10 = carbon chain <containing 1-8 C>
G11 = 37

G12 = OH
G23 = NH
G24 = phenylene (opt. substd. by (1) G25)
G31 = 168

L6 ANSWER 23 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)

G32 = phenylene (substd. by (1) G9)
Patent location: claim 9
Note: substitution is restricted

L6 ANSWER 24 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 134:366680 MARPAT
TITLE: Oncolytic combinations for the treatment of cancer
INVENTOR(S): Fleisch, Jerome Herbert; Benjamin, Roger Stuart; Sawyer, Jason Scott; Teicher, Beverly Ann; Beight, Douglas Wade; Smith, Edward C. R.; McMillen, William Thomas
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 283 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

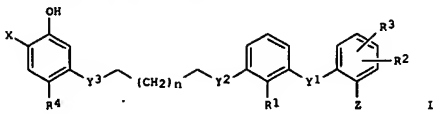
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034137	A2	20010517	WO 2000-US31039	20001109
WO 2001034137	A3	20020214		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2391416	AA	20010517	CA 2000-2391416	20001109
AU 2001015990	A5	20010606	AU 2001-15990	20001109
AU 778829	B2	20041223		
BR 2000015490	A	20020709	BR 2000-15490	20001109
EP 1231938	A2	20020821	EP 2000-978535	20001109
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003513916	T2	20030415	JP 2001-536137	20001109
NZ 517667	A	20040528	NZ 2000-517667	20001109
TR 200201245	T2	20040823	TR 2002-2002012452	20001109
ZA 2002002822	A	20030710	ZA 2002-2822	20020410
NO 2002002245	A	20020709	NO 2002-2245	20020510

PRIORITY APPLN. INFO.: US 1999-164786P 19991111
WO 2000-US31039 20001109
GI

L6 ANSWER 24 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)



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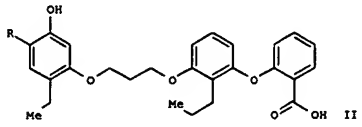
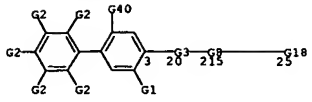


II

AB A method of treating cancer by administration of a 2',2'-difluoronucleoside anti-cancer compound and a leukotriene LTB4 inhibitor (I)
[wherein X = a 5-membered (un)substituted heterocycle or fused bicyclic radical consisting of a carbocyclic group fused to 2 adjacent C atoms of a
5-membered (un)substituted heterocycle; Y1 = a bond or divalent linking group containing 1-9 atoms; Y2 and Y3 = independently CH2, O, or S; Z = an
acidic group; R1 = (alk)aryl, cycloalkyl, (ar)alkyl, (ar)alkenyl, alkynyl,
haloalkyl, aryloxy, or alkoxy; R2 = H, halo(alkyl), alkoxy, (cyclo)alkyl, acidic group, or (CH2)1-7-acidic group; R3 = (cyclo)alkyl,
(CH2)1-7-cycloalkyl, alkenyl, alkynyl, benzyl, or aryl; n = 0-6] is disclosed. Examples includes 17 syntheses, 22 formulations, and mouse xenograft test results. For instance, benzylation of 1-[2-hydroxy-4-(3-chloropropoxy)-5-ethylphenyl]ethanone (69%), coupling the ethanone with 2-(3-hydroxy-2-propylphenoxy)benzoic acid Me ester (72%), oxidation to give
the α-hydroxy ketone (31%), cyclization with triflic anhydride and formamide to give the oxazole (6%), debenzylation with BF3•OEt2 (45%), and deesterification (92%) afforded II (R = 4-oxazolyl). Treatment of mice with 100 mg/kg of the LTB4 antagonist, 2-[2-propyl-3-[3-[2-ethyl-5-hydroxy-4-(4-fluorophenyl)phenoxy]propoxy]phenoxy]benzoic acid (II; R = 4-FC6H4) and 60 mg/kg of gemcitabine•HCl delayed growth of LNCaP prostate carcinoma by an average of 51.2 days, compared to a delay of 12.2
days using the gemcitabine•HCl alone.

MSTR 3

L6 ANSWER 24 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)



G10 = carbon chain <containing 1-8 C>
G11 = 37

G12 = OH
G23 = NH
G24 = phenylene (opt. substd. by (1) G25)
G31 = 168

G32 = phenylene (substd. by (1) G9)
Patent location: claim 12
Note: substitution is restricted

L6 ANSWER 25 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 134:366679 MARPAT
TITLE: Oncolytic combinations for the treatment of cancer
INVENTOR(S): Fleisch, Jerome Herbert; Sawyer, Jason Scott; Teicher,
Beverly Ann; Beight, Douglas Wade; Smith, Edward C. R.; McMillen, William Thomas
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 285 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034135	A2	20010517	WO 2000-US30944	20001109
WO 2001034135	A3	20020321		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2390789	AA	20010517	CA 2000-2390789	20001109
EP 1231939	A2	20020821	EP 2000-983695	20001109
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003513914	T2	20030415	JP 2001-536135	20001109

PRIORITY APPLN. INFO.: US 1999-164713P 19991111
WO 2000-US30944 20001109

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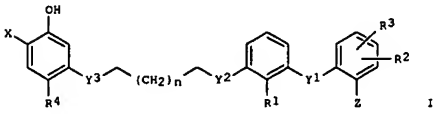

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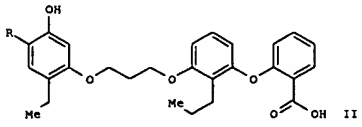
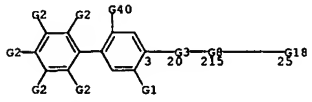


II

L6 ANSWER 25 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)

AB A method of treating cancer with therapeutic combinations of a leukotriene
LTB4 inhibitor (I) [wherein X = a 5-membered (un)substituted heterocycle or fused bicyclic radical consisting of a carbocyclic group fused to 2 adjacent C atoms of a 5-membered (un)substituted heterocycle; Y1 = a bond or divalent linking group containing 1-9 atoms; Y2 and Y3 = independently CH2,
O, or S; Z = an acidic group; R1 = (alk)aryl, cycloalkyl, (ar)alkyl, (ar)alkenyl, alkynyl, haloalkyl, aryloxy, or alkoxy; R2 = H, halo(alkyl), alkoxy, (cyclo)alkyl, acidic group, or (CH2)1-7-acidic group; R3 = (cyclo)alkyl, (CH2)1-7-cycloalkyl, alkenyl, alkynyl, benzyl, or aryl; n = 0-6] and an anti-cancer agent is disclosed. Examples includes 17 syntheses, 7 formulations, and nude mouse xenograft test results. For instance, benzylation of 1-[2-hydroxy-4-(3-chloropropoxy)-5-ethylphenyl]ethanone (69%), coupling the ethanone with 2-(3-hydroxy-2-propylphenoxy)benzoic acid Me ester (72%), oxidation to give
the α-hydroxy ketone (31%), cyclization with triflic anhydride and formamide to give the oxazole (6%), debenzylation with BF3•OEt2 (45%), and deesterification (92%) afforded II (R = 4-oxazolyl). Treatment of mice with 200 mg/kg of the LTB4 antagonist, 2-[2-propyl-3-[3-[2-ethyl-5-hydroxy-4-(4-fluorophenyl)phenoxy]propoxy]phenoxy]benzoic acid (II; R = 4-FC6H4) and 50 mg/kg of carboplatin delayed growth of human H460 non-small cell lung carcinoma by an average of 33.3 days, compared to a delay
of 13.9 days using the leukotriene antagonist alone or 10.7 days using carboplatin alone.

MSTR 2



G10 = carbon chain <containing 1-8 C>
G11 = 37

G12 = OH
G23 = NH
G24 = phenylene (opt. substd. by (1) G25)
G31 = 168

L6 ANSWER 25 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)

G32 = phenylene (substd. by (1) G9)
Patent location: claim 8
Note: substitution is restricted

L6 ANSWER 26 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 134:63801 MARPAT
TITLE: Black-and-white photographic developer
INVENTOR(S): Kirsten, Nikolaus
PATENT ASSIGNEE(S): Agfa-Gevaert Naamloze Vennootschap, Belg.
SOURCE: Eur. Pat. Appl., 13 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1061415	A1	20001220	EP 2000-202104	20000614
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
DE 19939392	A1	20001221	DE 1999-19939392	19990819

PRIORITY APPLN. INFO.: DE 1999-19928157 19990619
DE 1999-19939392 19990819

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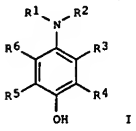
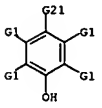


I

AB The black and white photog. developer comprises a combination of (a) ascorbic acid salt or isoascorbic acid salt and (b) a compound represented by a formula I (R1-6 = H, alkyl, alkoxy, aryloxy, etc.) as well as 1-phenyl-5-mercaptotetrazole as a stabilizer. The hydroquinone-free developer produces images with high maximum d., low min. d., and blue-black image tone.

MSTR 1



L6 ANSWER 26 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
G1 = 45

G2 = NH
G5 = phenylene
G7 = alkylene <containing 1-3 C, unbranched>
G14 = CO2H
Patent location: claim 1

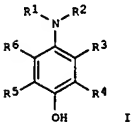
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L6 ANSWER 27 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 134:63797 MARPAT
TITLE: Black-and-white photographic developer
INVENTOR(S): Kirsten, Nikolaus
PATENT ASSIGNEE(S): Agfa-Gevaert A.-G., Germany
SOURCE: Ger. Offen., 10 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19939392	A1	20001221	DE 1999-19939392	19990819
EP 1061415	A1	20001220	EP 2000-202104	20000614
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: DE 1999-19928157 19990619
DE 1999-19939392 19990819

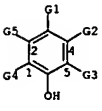
GI



I

AB The black-and-white photog. developer comprises a combination of (a) ascorbic acid salt or isoascorbic acid salt and (b) a compound represented by a formula I (R1-6 = H, alkyl, alkoxy, aryloxy, etc.) as well as 1-phenyl-5-mercaptotetrazole as a stabilizer. The hydroquinone-free developer produces images with high maximum d., low minium d. and blue-black image toner.

MSTR 1



G13 = CO2H
G15 = alkylene <containing 1-3 C, unbranched>
G22 = NH (opt. substd.)
G29 = phenylene

L6 ANSWER 27 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
G42 = phenylene
Patent location: claim 1
Note: additional ring formation also claimed
Note: or salts

L6 ANSWER 28 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 133:335164 MARPAT
TITLE: Tri-aryl acid derivatives as PPAR receptor ligands
INVENTOR(S): Jayyosi, Zaid; McGeehan, Gerard M.; Kelley, Michael F.; Labaudiniere, Richard F.; Zhang, Litao; Caulfield, Thomas J.; Minnich, Anne; Bobko, Mark; Morris, Robert; Groneberg, Robert D.; Mcgarry, Daniel G.
PATENT ASSIGNEE(S): Aventis Pharmaceuticals Products Inc., USA
SOURCE: PCT Int. Appl., 257 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000064876	A1	20001102	WO 2000-US11490	20000428
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
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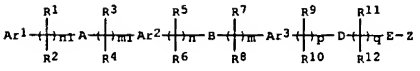
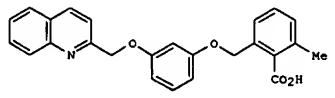
CA 2371308	AA	20001102	CA 2000-2371308	20000428
EP 1177176	A1	20020206	EP 2000-930210	20000428
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
BR 2000010126	A	20020226	BR 2000-10126	20000428
EE 200100558	A	20021216	EE 2001-558	20000428
NZ 515087	A	20031128	NZ 2000-515087	20000428
AU 782404	B2	20050728	AU 2000-48070	20000428
ZA 2001008800	A	20030210	ZA 2001-8800	20011024
NO 2001005226	A	20011205	NO 2001-5226	20011025
HR 2001000793	A1	20030228	HR 2001-793	20011026
HK 1047098	A1	20050520	HK 2002-108625	20021129
PRIORITY APPLN. INFO.:			US 1999-131454P	19990428
			WO 2000-US11490	20000428

GI

L6 ANSWER 28 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)



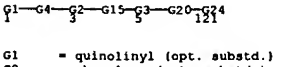
I



II

AB This invention is directed to triaryl acid derivs. I and their salts, N-oxides, hydrates, solvates, and pharmaceutical compns. [wherein: Ar1, Ar2, Ar3 = aryl, fused arylcycloalkenyl, fused arylcycloalkyl, fused arylheterocyclenyl, fused arylheterocyclyl, heteroaryl, fused heteroarylcycloalkemyl, fused heteroarylcycloalkyl, fused heteroarylheterocyclenyl, or fused heteroarylheterocyclyl; A = bond, O, S, SO, SO2, CO, (un)substituted NH, NHCO, CONH, NHCONH, CH:N, etc.; B = bond, O, S, SO, SO2, C.tplbond.C, CO, (un)substituted NH, NHCO, or CONH; D = bond, O, S, C.tplbond.C, CO, (un)substituted NH, NHCO, or CONH; E = bond, CH2CH2; Z = (un)substituted CO2H, CHO, cyclo-imide, cyano, sulfonylaminocarbonyl, sulfonylamino, carbamoyl, tetrazolyl, etc.; R1, R3, R5, R7, R9, R11 = H, halo, alkyl, CO2H, alkoxycarbonyl, aralkyl; R2, R4, R6, R8, R10, R12 = (CH2)0-3X (where X = H or various substituents); n1 = 0-4; m1 = 0-4; n = 0-4; m = 0-5; p = 0-4; q = 0-6; with numerous provisos]. The compds. are PPAR receptor ligands, useful as agonists or antagonists thereof (no data). For instance, 2,6-dimethylbenzoic acid underwent a sequence of: (1) Me esterification, (2) benzylic monobromination, (3) etherification with 3-(quinolin-2-ylmethoxy)phenol, and (4) alkaline hydrolysis with NaOH in aqueous EtOH, to give title compound II.

MSTR 1



G1 = quinolinyl (opt. substd.)
G2 = phenylene (opt. substd.)
G3 = o-C6H4 (opt. substd.)
G15 = NH (opt. substd.)
G20 = carbon chain <containing 1 or more C, 0-1 triple bond, 0 or more double bonds> (opt. substd.)
G24 = 145

L6 ANSWER 28 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)

G25 = OH
Patent location: claim 1
Note: additional ring formation also claimed
Note: or pharmaceutically acceptable salts, N-oxides, hydrates or solvates

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 29 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 133:281779 MARPAT
TITLE: Preparation of aryl substituted pyrazoles, imidazoles, oxazoles, thiazoles and pyrroles as sodium channels blockers
INVENTOR(S): Hogenkamp, Derk J.; Upasani, Ravindra; Nguyen, Phong
PATENT ASSIGNEE(S): Cocensys, Inc., USA
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000057877	A1	20001005	WO 2000-US7944	20000324
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2368631	AA	20001005	CA 2000-2368631	20000324
EP 1173169	A1	20020123	EP 2000-919636	20000324
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000009322	A	20020430	BR 2000-9322	20000324
TR 200102790	T2	20020621	TR 2001-200102790	20000324
US 6414011	B1	20020702	US 2000-533864	20000324
DE 20080291	U1	20020801	DE 2000-20080291	20000324
TW 502019	B	20020911	TW 2000-89105616	20000324
JP 2002540155	T2	20021126	JP 2000-607628	20000324
NZ 514756	A	20040430	NZ 2000-514756	20000324
AU 782353	B2	20050721	AU 2000-40291	20000324
NO 2001004659	A	20011101	NO 2001-4659	20010925
ZA 2001008807	A	20021025	ZA 2001-8807	20011025
US 2003069292	A1	20030410	US 2002-134697	20020430
US 6737418	B2	20040518		
NZ 529690	A	20031219	NZ 2003-529690	20031121
PRIORITY APPLN. INFO.:			US 1999-126553P	19990326
			US 2000-533864	20000324
			WO 2000-US7944	20000324

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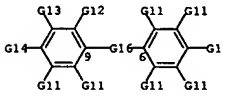
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; Het = II-IV, etc.; R1 = H, alkyl, cycloalkyl, etc.; R2, R3 = H, alkyl, cycloalkyl, etc.; R5-R13 = H, halo, haloalkyl, etc.; X

L6 ANSWER 29 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
= O, S, CH2, NH, etc.] and their pharmaceutically acceptable salts which act as sodium channel blockers, and are useful as anticonvulsants, were prepd. E.g. a 3-step synthesis of V which showed ED50 of 4.2 mg/kg (p.o.) against MES, was given.

MSTR 1



G1 = 16

G12 = alkyl <containing 1-10 C> (substd. by G15)
G15 = CO2H
G16 = NH
Patent location: claim 1
Note: substitution is restricted
Note: or pharmaceutically acceptable salts, prodrugs or solvates
Note: additional ring formation also claimed
Note: or radiolabeled derivatives

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 30 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 133:4529 MARPAT
TITLE: Preparation of biphenyl and naphthalene compounds as β-amyloid protein production/secretion inhibitors
INVENTOR(S): Kato, Kaneyoshi; Terauchi, Jun; Fukumoto, Hiroaki; Kakihana, Mitsuru
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 182 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000031021	A1	20000602	WO 1999-JP6450	19991118
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2351692	AA	20000602	CA 1999-2351692	19991118
JP 2000212076	A2	20000802	JP 1999-327823	19991118
EP 1132376	A1	20010912	EP 1999-972620	19991118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6586475	B1	20030701	US 2001-856317	20010605
PRIORITY APPLN. INFO.:			JP 1998-331018	19981120
			WO 1999-JP6450	19991118

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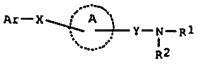
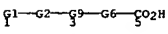


I

AB The title compds. I [Ar represents an aromatic group; X and Y represent each a divalent group selected from among O, S, CO, SO, SO2, NR8, CONR8, SO2NR8 and COO (wherein R8 represents H, hydrocarbyl or acyl), or divalent aliphatic C1-6 hydrocarbyl optionally containing one or two of these divalent groups; R1 and R2 represent each H or C1-6 alkyl, or R1 and R2 may form together with the nitrogen atom a nitrogen-containing heterocycle; and the ring A represents a monocyclic aromatic ring] are prepared 4-(4-Biphenylylmethoxy)-N-(2-piperidinoethyl)benzamide at 10 μM gave 39% inhibition of Aβ1-40 production/secretion. Formulations are given.

MSTR 4

L6 ANSWER 30 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)



G1 = 57

G2 = NH
G6 = alkylene <containing 1 or more C, unbranched>
G9 = phenylene (opt. substd. by 1 or more G10)
Derivative: or salts
Patent location: claim 34

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 31 OF 59 MARPAT COPYRIGHT 2005 ACS on STN

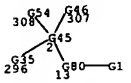
ACCESSION NUMBER: 132:175862 MARPAT
TITLE: Treatment of ischemia with an angiotensin II antagonist
INVENTOR(S): Avkran, Metin
PATENT ASSIGNEE(S): United Medical and Dental Schools of Guy's and St. Thomas's Hospitals, UK
SOURCE: Brit. UK Pat. Appl., 59 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2337701	A1	19991201	GB 1998-11312	19980526

PRIORITY APPLN. INFO.: GB 1998-11312 19980526

AB A method for modulating intracellular pH and/or cellular ion transport to confer protective effects of angiotensin II receptor antagonists in patients with or at risk for myocardial, cerebral and kidney tissue ischemia is described. For example, losartan inhibited an increase in sarcolemmal Na+/H+ exchanger activity induced by the angiotensin II/PD123319 combination in rat ventricular myocytes and confirmed that exchanger stimulation by this intervention is mediated selectively via the AT1 receptor subtype. Thus, selective antagonists of the AT1 receptor, such as losartan, may exhibit cardioprotective actions.

MSTR 1



G10 = NH (opt. substd.)
G18 = 103

G19 = CO2H (opt. substd.)
G24 = 95-65 94-102

L6 ANSWER 31 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)

G31 = p-C6H4 (opt. substd.)
G45 = 309-296 3-13 5-308 4-307

Derivative: and pharmaceutically acceptable salts
Patent location: claim 4
Note: substitution is restricted

L6 ANSWER 32 OF 59 MARPAT COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 132:137377 MARPAT
TITLE: Preparation of benzoxazolyl piperidines and analogs as rotamase enzyme inhibitors
INVENTOR(S): Kemp, Mark Ian; Palmer, Michael John; Sanner, Mark Allen; Wythes, Martin James
PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.
SOURCE: PCT Int. Appl., 131 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000005232	A1	20000203	WO 1999-IB1211	19990628
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2338214	AA	20000203	CA 1999-2338214	19990628
AU 9942858	A1	20000214	AU 1999-42858	19990628
AU 765925	B2	20031002		
BR 9912330	A	20010417	BR 1999-12330	19990628
EP 1100797	A1	20010523	EP 1999-963123	19990628
EP 1100797	B1	20030226		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
TR 200100135	T2	20010621	TR 2001-200100135	19990628
EE 200100044	A	20020617	EE 2001-44	19990628
JP 2002521382	T2	20020716	JP 2000-561188	19990628
NZ 508838	A	20021220	NZ 1999-508838	19990628
AT 233261	E	20030315	AT 1999-963123	19990628
ES 2191484	T3	20030901	ES 1999-963123	19990628
NZ 522270	A	20040326	NZ 1999-522270	19990628
CN 1511837	A	20040714	CN 2003-10123907	19990628
NO 2001000322	A	20010315	NO 2001-322	20010119
HR 2001000052	A1	20011231	HR 2001-52	20010119
BG 105254	A	20011031	BG 2001-105254	20010214
JP 2004002374	A2	20040108	JP 2003-105099	20030409

PRIORITY APPLN. INFO.: GB 1998-15880 19980721
JP 2000-561188 19990628
NZ 1999-508838 19990628
WO 1999-IB1211 19990628

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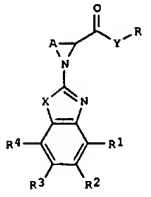
L6 ANSWER 32 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)



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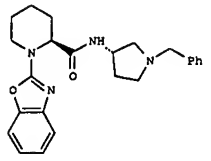
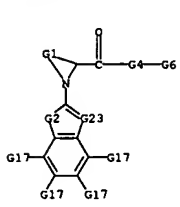


II

AB Title compds. (I) [wherein A = (un)substituted unbranched C3-C5 alkylene; X and Y = independently O, S, NH, or N-alkyl; R = (un)substituted, C-linked, 4- to 6-membered, non-aromatic, heterocyclic ring containing 1 N; R1-R4 = independently H, halo, (cyclo)alkyl, haloalkyl, (cyclo)alkoxy, CONR5R6, cycloalkylalkylene, cycloalkylalkoxy, or CO2R7; R5 and R6 = independently H, alkyl, or taken together = unbranched alkylene; R7 = alkyl] were prepared as rotamase enzyme inhibitors, particularly FKBP-12 and FKBP-52 inhibitors. Thus, (2S)-1-(1,3-benzoxazol-2-yl)-2-piperidinecarboxylic acid (preparation given) was amidated with (3S)-1-benzylpyrrolidine-3-ylamine in the presence of 1-hydroxybenzotriazole hydrate and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide.HCl in CH2Cl2 to yield II. Twenty-one compds. of the invention demonstrated inhibitory activity against human recombinant FKBP-12 in a coupled colorimetric PPIase in vitro assay with IC50 values below 1200 nM, and II inhibited the rotamase enzyme FKBP-52 in a similar assay with IC50 = 2790 nM. As neurotrophic agents, the invention compds. promote neuronal regeneration and outgrowth and are useful for the treatment of neurodegenerative diseases or other disorders involving nerve damage.

MSTR 1



G7 = alkyl <containing 1-6 C>

L6 ANSWER 32 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
(opt. substd. by (1-2) G12)
G8 = alkylamino <containing 1-6 C> / azetidino
G12 = Ph (opt. substd. by (1-3) G8) / 29

Derivative: or pharmaceutically acceptable salts
Patent location: claim 1

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L6 ANSWER 33 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 131:243084 MARPAT
TITLE: Preparation of naphthyl and indolyl acylsulfonamides for the treatment and prevention of prostaglandin mediated disease
INVENTOR(S): Gareau, Yves; Labelle, Marc; Juteau, Helene; Gallant, Michel; Lachance, Nicolas; Belley, Michel
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 143 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9947497	A2	19990923	WO 1999-CA212	19990312
WO 9947497	A3	19991028		
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6242493	B1	20010605	US 1999-266047	19990310
CA 2322742	AA	19990923	CA 1999-2322742	19990312
AU 9927086	A1	19991011	AU 1999-27086	19990312
AU 756333	B2	20030109		
EP 1071648	A2	20010131	EP 1999-907214	19990312
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2002506851	T2	20020305	JP 2000-536694	19990312

PRIORITY APPLN. INFO.: US 1998-77990P 19980313
GB 1998-15856 19980721
WO 1999-CA212 19990312

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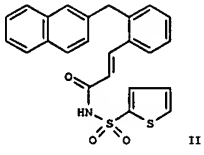
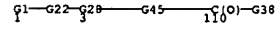


II

AB Naphthyl and indolyl acylsulfonamides (I) [where HET = 5-12 membered monocyclic or bicyclic aromatic ring with 1-3 O, S(O)n, or N(O)m heteroatoms;

L6 ANSWER 33 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
A = O, S(O)n, (un)substituted NH, C(O), (un)substituted CH2, CH2-CH2 or CH=CH, etc.; B = (un)substituted (CH2)p-Y-(CH2)q; X = (un)substituted 5-10 membered monocyclic or bicyclic (hetero)aryl with 1-3 O, S(O)n, or N(O)m heteroatoms; Y = O, S(O)n, (un)substituted NH, a bond, or (un)substituted CH=CH; Z = OH or NH-SO2R4; R1, R2, and R3 = independently H, halogen, alkyl, alkenyl, (heteroaryl)alkynyl, (un)substituted (CH2)pS(O)nH, (CH2)pOH, or (CH2)pNH2, CN, NO2, CO2H or ester, (un)substituted C(O)-NH2; R4 = (heteroaryl)alkyl, (heteroaryl)alkenyl, alkynyl, CF3, heteroaryl; m = 0 or 1; n = 0-2; p and q = independently 0-3 and p + q = 0-6], as well as pharmaceutically acceptable salts, hydrates and esters thereof, were prepd. as antagonists of the pain and inflammatory effects of E-type prostaglandins. For instance, Et (E)-3-[2-(bromomethyl)phenyl]-2-propenoate (prepn. given) was treated with 2-naphthylboronic acid, followed by hydrolysis of the ester to give (E)-3-[2-(2-naphthylmethyl)phenyl]-2-propenoic acid. The acid was coupled with 2-thiophenesulfonamide to yield N-[(E)-3-[2-(2-naphthylmethyl)phenyl]-2-propenoyl]-2-thiophenesulfonamide (II). Compds. of the invention were reported to have demonstrated prostanoid antagonist or agonist activity and selectivity through a variety of in vitro and in vivo prostanoid receptor assays (no data). Testing against edema, pyrexia, inflammation, and arthritis was also discussed (no data). The compds. are claimed to be useful as analgesics, antipyretic agents, antiinflammatory agents, and antitumor agents for the treatment or prevention of prostaglandin mediated disease.

MSTR 1



G1 = biphenylyl
G22 = NH
G28 = phenylene (opt. substd. by 1 or more G47)
G38 = OH
G45 = carbon chain <containing 1 or more C, 0-1 double bond, no triple bonds> (opt. substd. by 1 or more G14)
Derivative: or pharmaceutically acceptable salts, hydrates or esters
Patent location: claim 1
Note: additional ring formation also claimed
Note: substitution is restricted

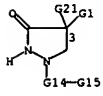
L6 ANSWER 34 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 131:151652 MARPAT
TITLE: 3-pyrazolidone compounds and photographic developer solutions containing same
INVENTOR(S): Roussilhe, Jacques; Tsoi, Siu C.
PATENT ASSIGNEE(S): Eastman Kodak Co., USA
SOURCE: U.S., 16 pp., Cont.-in-part of U. S. Ser. No. 694,792, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5942379	A	19990824	US 1998-10302	19980121
FR 2737722	A1	19970214	FR 1995-9850	19950810
FR 2737722	B1	19970905		

PRIORITY APPLN. INFO.: FR 1995-9850 19950810
US 1996-694792 19960809

AB The present concerns compds. of the 3-pyrazolidone type comprising solubilizing groups which are not directly attached to the Ph ring or to the pyrazolidino ring. These compds. can be used as codeveloping agents in the development of black-and-white photog. products.

MSTR 1



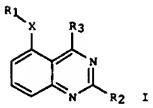
G7 = alkylene <containing 1-3 C, unbranched>
G10 = CO2H
G14 = phenylene (opt. substd. by G20)
G16 = NH (opt. substd.)
G24 = phenylene
Patent location: claim 1
Note: substitution is restricted

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L6 ANSWER 35 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 130:10618 MARPAT
TITLE: Modulating serine/threonine protein kinase function with quinazoline-based compounds and their use as antitumor and anti-fibrotic agents
INVENTOR(S): Tang, Peng C.; McMahon, Gerald; Weinberger, Heinz; Kutscher, Bernhard; App, Harald
PATENT ASSIGNEE(S): Sugen, Inc., USA
SOURCE: PCT Int. Appl., 147 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9850370	A1	19981112	WO 1998-US9060	19980501
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9803669	A	19991101	ZA 1998-3669	19980430
CA 2288778	AA	19981112	CA 1998-2288778	19980501
AU 9872829	A1	19981127	AU 1998-72829	19980501
EP 981519	A1	20000301	EP 1998-920203	19980501
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6204267	B1	20010320	US 1998-71682	19980501
JP 2001524128	T2	20011127	JP 1998-548336	19980501
US 2001014679	A1	20010816	US 2001-769360	20010126
US 6911446	B2	20050628		

PRIORITY APPLN. INFO.: US 1997-45351P 19970502
US 1997-60152P 19970926
US 1998-71682 19980501
WO 1998-US9060 19980501
OTHER SOURCE(S): CASREACT 130:10618
GI

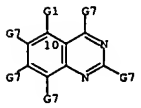


I

L6 ANSWER 35 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

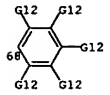
L6 ANSWER 35 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
AB The present invention is directed in part towards methods of modulating the function of serine/threonine protein kinases with quinazoline-based compds (I). The methods incorporate cells that express a serine/threonine protein kinase, such as RAF. In addition, the invention describes methods of preventing and treating serine/threonine protein kinase-related abnormal conditions (e.g., tumors, fibrotic disorders, or other signal transduction aberrations) in organisms with a compound identified by the invention. Furthermore, the invention pertains to quinazoline compds. and pharmaceutical compns. comprising these compds. Syntheses and biol. activities are are provided for 38 quinazoline-based compds.

MSTR 1

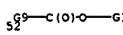


G2 = 15

G6 = 68



G7 = Ph (opt. substd.)
G9 = carbon chain (opt. substd.)
G12 = 52



Patent location: claim 10
Note: additional ring formation also claimed
Note: also incorporates claim 34

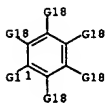
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS

L6 ANSWER 36 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 129:100056 MARPAT
TITLE: Anti-amyloidogenic agents
INVENTOR(S): De Guzman Mirov, Greta J.; Kelly, Jeffery W.; Lai, Zhihong; Lashuel, Hilal A.; Peterson, Scott A.
PATENT ASSIGNEE(S): Texas A & M University, USA
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

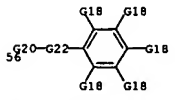
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9827972	A2	19980702	WO 1997-US24181	19971223
WO 9827972	A3	19990218		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9857277	A1	19980717	AU 1998-57277	19971223

PRIORITY APPLN. INFO.: US 1996-771938 19961223
WO 1997-US24181 19971223
AB A method for treating a human amyloid disease which includes administering a pharmaceutically effective amount of a composition including an amyloidogenic protein-stabilizing aryl compound Examples are given for the preparation of Me N-phenyl-2-aminobenzoate and inhibition of amyloid fibril formation with fenoprofen and flufenamic acid.

MSTR 1



G1 = 56



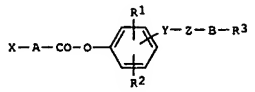
G5 = alkylene <containing 1-6 C>

L6 ANSWER 36 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
(opt. substd. by 1 or more G19)
G6 = CO2H
G18 = Ph
G20 = NH
Patent location: claim 1
Note: alkyl and alkenyl moieties may also be cyclic; substitution is restricted

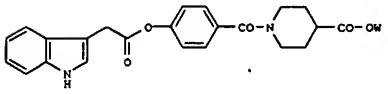
L6 ANSWER 37 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 128:321560 MARPAT
TITLE: Preparation of phenol ester derivatives as chymase inhibitors
INVENTOR(S): Tamura, Norikazu; Mori, Masaaki; Irie, Kazuyuki; Fujisawa, Yukio
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 32 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10087567	A2	19980407	JP 1997-146555	19970604
PRIORITY APPLN. INFO.:			JP 1996-142823	19960605

GI



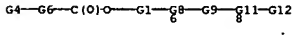
I



II

AB The title compds. [I; R1, R2 = H, OH, (un)substituted alkyl or alkoxy; R3 = acyl, esterified CO2, etc.; X = cyclyl, or heterocyclyl; A = bond, (un)substituted alkylene or imino; Y = CO, SO2, (un)substituted alkylene or imino; Z = (un)substituted phenylene, heterocyclyl, etc.; B = bond, lower alkylene, phenylene] are prepared I, possessing chymase inhibitory activity, are useful as cardiovascular agents. Thus, compound (II; W = C6H5CH2) (preparation given) was hydrogenated over Pd/C to give the title compound II (W = H), which showed IC50 of 0.038 X 10-6 M against human chymase.

MSTR 1



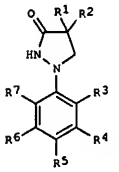
L6 ANSWER 37 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)

G1 = phenylene (opt. substd. by (up to 2) G2)
G2 = loweralkyl (opt. substd. by (up to 4) G3)
G3 = CO2H
G8 = NH
G9 = phenylene (opt. substd. by (up to 5) G10)
G11 = phenylene
Derivative: or salts
Patent location: claim 1
Note: also incorporates claim 18

L6 ANSWER 38 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 128:263873 MARPAT
TITLE: Developer composition for photographic silver halide emulsion, containing ascorbic acid-type developer and accelerator
INVENTOR(S): Roussilhe, Jacques; Tsoi, Siu-Chung
PATENT ASSIGNEE(S): Eastman Kodak Co., USA
SOURCE: Ger. Offen., 20 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19738120	A1	19980326	DE 1997-19738120	19970901
FR 2753812	A1	19980327	FR 1996-11958	19960925
FR 2753812	B1	20040116		
JP 10104805	A2	19980424	JP 1997-258513	19970924
US 5837434	A	19981117	US 1997-936406	19970925
PRIORITY APPLN. INFO.:			FR 1996-11958	19960925

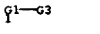
GI



I

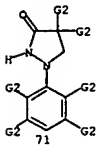
AB The title hydroquinone-free aqueous composition, for developing photog. Ag halide,
comprised of an ascorbic acid-type developer for Ag halides, at least 1 phenidone-type auxiliary developer and at least 1 development accelerator,
the auxiliary developer has a following formula I (R1-7 = H, alkyl, alkoxy, aryloxy, etc.) and the development accelerator is either thioether
with at least 1 amino group, triazolium-thiolate, or substituted thio-alkane. The developer composition is suitable for developing black-and-white materials especially radiog. or graphic arts.

MSTR 1



G1 = 71

L6 ANSWER 38 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)

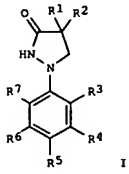


G11 = (1-3) CH2
G12 = NH (opt. substd.)
G14 = phenylene
G23 = CO2H
Patent location: claim 1

L6 ANSWER 39 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 128:121618 MARPAT
TITLE: Composition for photographic development containing codeveloper of the type 1-phenyl-3-pyrazolidone
INVENTOR(S): Roussilhe, Jacques; Tsoi, Siu Chung
PATENT ASSIGNEE(S): Kodak Pathe S. A., Fr.; Kodak Ltd.
SOURCE: Fr. Demande, 26 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2750225	A1	19971226	FR 1996-8149	19960624
FR 2750225	B1	19990924		
EP 816916	A1	19980107	EP 1997-420091	19970617
EP 816916	B1	20040811		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 5780212	A	19980714	US 1997-881408	19970624

PRIORITY APPLN. INFO.: FR 1996-8149 19960624
GI



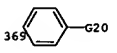
I

AB The title developer composition comprises a codeveloper of the type I [R1, R2 = alkyl, A-Xp-A-Sol; R3-R7 = H, alkyl, alkoxy, aryloxy, Xp-A-Sol where p = 0, 1; X = divalent group from O, S, NR8; R8 = H, alkyl, A-Sol; A = C0-5-alkylene, phenylene, -(CH2)yC6H4-, -C6H4(CH2)y-; y = 1-3; Sol = solubilizing group from CO2H, SO3H, NHSO2R10, SO2NH2, SO2NHR10, polyhydroxyalkyl, -CH(SO3H)COR11, -COCH(SO3H)R12, -CH(SO3H)CN, R10 = alkyl, aryl; R11 = OH, alkyl, aryl; R12 = H, alkyl, aryl; with the condition that ≥1 of R1-R7 must contain a Sol group and Xp-A-Sol can not be a methylsulfonamidophenyl group]. The primary developer can be selected from hydroquinone and its derivs. and ascorbic acid, its derivs., precursors, stereoisomers, or its salts. The codevelopers improve the stability of the developer.

L6 ANSWER 39 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)

NSTR 1

G5 = NH
G7 = alkylene <containing 1-5 C, unbranched>
G8 = CO2H
G13 = 369

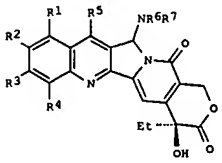


G23 = phenylene
Patent location: claim 1
Note: substitution is restricted

L6 ANSWER 40 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 128:75575 MARPAT
TITLE: Preparation of water-soluble C-ring analogs of 20(S)-camptothecin
INVENTOR(S): Duvvuri, Subrahmanyam; Akella, Venkateswarlu; Vedula, Sharma Manohara; Kulakarni, Archana Prabhakar
PATENT ASSIGNEE(S): Dr. Reddy's Research Foundation, India; Reddy-Cheminor, Inc.
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9746562	A1	19971211	WO 1997-US6960	19970422
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5972955	A	19991026	US 1996-771390	19961219
ZA 9703158	A	19971106	ZA 1997-3158	19970414
ZA 9703159	A	19981014	ZA 1997-3159	19970414
AU 9728124	A1	19980105	AU 1997-28124	19970422
EP 906317	A1	19990407	EP 1997-922465	19970422
R: CH, DE, FR, GB, LI, SE				
JP 2000511556	T2	20000905	JP 1998-500567	19970422

PRIORITY APPLN. INFO.: US 1996-655259 19960605
US 1996-771390 19961219
US 1995-471640 19950606
WO 1997-US6960 19970422
GI

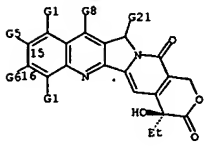


I

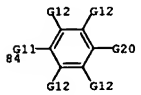
AB Novel water-soluble C-ring analogs of 20(S)-camptothecin I (R1-R4 = H, HO, alkoxy, aryloxy, alkanoyl, nitro, cyano, halo, carboxy, carbonyloxy, amino, substituted amino, alkyl, substituted alkyl; R2R3 may form

L6 ANSWER 40 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
O(CH2)nO, n = 1, 2; R5 = H, alkyl, aralkyl, hydroxymethyl, carboxymethyl, aminomethyl, substituted aminomethyl; R6 = H, alkyl, alkenyl, alkanoyl, alkenyl, alkoxycarbonyl, (un)substituted Ph, benzyl, or benzoyl; R7 = H, HO, alkoxy, carboxy, alkoxycarbonyl, carbamoyl, R6R7N may form a ring) were prepd. as anti-cancer and anti-viral agents. Thus 5-hydroxycamptothecin was treated with 2-aminoethanol to give 5-(2-amnioethylamino)camptothecin. The anticancer IC50 of 5-(methylamino)camptothecin was .22 μm against leukemia HL 60.

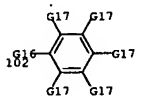
MSTR 1



G10 = 84



G13 = 102



G17 = alkyl <containing 1 or more C>
(opt. substd. by 1 or more G22)
G20 = Ph
G21 = 75

L6 ANSWER 40 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
G22 = CO2H
Patent location: claim 1
Note: also incorporates claim 18

L6 ANSWER 41 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 126:205442 MARPAT
TITLE: Process for preparation of amine compound for use in electrophotography
INVENTOR(S): Nukada, Katsumi
PATENT ASSIGNEE(S): Fuji Xerox Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 57 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

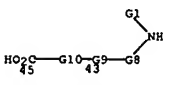
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 755916	A2	19970129	EP 1996-111678	19960719
EP 755916	A3	19971210		
EP 755916	B1	20010425		
R: DE, FR, GB				
JP 09031039	A2	19970204	JP 1995-206831	19950721
JP 3550813	B2	20040804		

PRIORITY APPLN. INFO.: JP 1995-206831 19950721
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A process for preparing an amine compound for use in preparing electrophotog.
photoreceptors comprises using a compound represented by formula I to obtain
an amine compound represented by formula II, III, or IV wherein R1-3 = H, alkyl, alkoxy, substituted amino, halogen, or aryl; R4 = H, alkyl, aryl, or aralkyl; G = Br or I; X = arylene; n = 0 or 1; T = a C1-10 hydrocarbon group; Y = aryl. The amine compound is used as a charge-transporting agent
in preparing electrophotog. photoreceptors.

MSTR 6

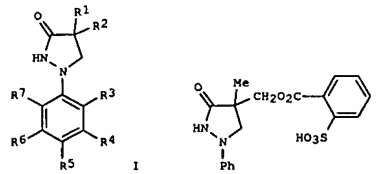


G1 = Ph (opt. substd. by (1-3) G11)
G8 = phenylene
G10 = carbon chain <containing 1-10 C>
G11 = Ph
Patent location: claim 3

L6 ANSWER 42 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 126:205409 MARPAT
TITLE: Preparation of 1-phenyl-3-pyrazolidone derivatives as photographic codevelopers
INVENTOR(S): Roussilhe, Jacques; Tsoi, Siu-Chung
PATENT ASSIGNEE(S): Eastman Kodak Company, USA
SOURCE: Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 758646	A1	19970219	EP 1996-420267	19960805
EP 758646	B1	20000426		
R: DE, FR, GB				
FR 2737722	A1	19970214	FR 1995-9850	19950810
FR 2737722	B1	19970905		
JP 09120121	A2	19970506	JP 1996-211692	19960809

PRIORITY APPLN. INFO.: FR 1995-9850 19950810
GI

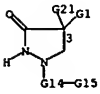


I II

AB The title compds. [I; R1, R2 = (un)substituted alkyl, (CH2)m(L)nA-(Sol); wherein m = 0-5; n = 0,1; L = O, S, NR8, O2C, CO2, OCO2, O2CNR8, CO, NR9CO, NR9SO2, NR9CONR9; wherein R8 = R9, A-(Sol); wherein R9 = H, alkyl, aryl; A = (CH2)q, phenylene, (CH2)yC6H4, C6H4 (CH2)y; wherein q = 0-5; y = 1-3; (Sol) = a solubilizing group selected from CO2H, SO3H, NHSO2R10, SO2NH2, SO2 NHR10, polyhydroxyalkyl, etc.; wherein R10 alkyl, aryl; R3 - R7 = H, (un)substituted alkyl, alkoxy, or aryloxy, (X)p (CH2)m (L)nA(Sol); wherein p = 0,1; m, L, A, (Sol) = same as above; provided that at least one of R1 - R7 must contain a group (Sol)] comprising solubilizing groups which are not directly attached to the Ph ring or to the pyrazolidino ring
are prepared These compds. can be used as codevelopers in the development
of black and white photog. papers or films. Thus, 2-sulfobenzoic acid cyclic anhydride was added to a suspension of 1-(3,4-dimethylphenyl)-4-hydroxymethyl-4-methyl-3-pyrazolidinone in MeCN with stirring and the reaction mixture was heated to reflux for 22 h to give 77% the title compound

L6 ANSWER 42 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
(II). According to the sensitometric curves, a developer soln. contg. ascorbic acid as a developer and II and a codeveloper was more active than
a developer contg. Elon assocd. ascorbic acid or hydroquinone.

MSTR 1

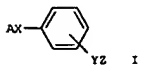


G7 = alkylene <containing 1-3 C, unbranched>
G10 = CO2H
G14 = phenylene (opt. substd. by 1 or more G20)
G16 = NH (opt. substd.)
G24 = phenylene
Patent location: claim 1
Note: substitution is restricted

L6 ANSWER 43 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 126:157280 MARPAT
TITLE: Preparation of aromatic alkanoic acid and alkanol derivatives as antithrombotics
INVENTOR(S): Hashizume, Hiroichi; Hagiwara, Masaki; Myamae, Tetsuhisa; Ogawa, Masaji; Ppongo, Tomoko; Morikawa, Tadanori
PATENT ASSIGNEE(S): Fuji Yakuhin Kogyo Kk, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 17 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

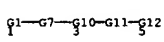
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08333287	A2	19961217	JP 1995-158813	19950602

PRIORITY APPLN. INFO.: JP 1995-158813 19950602
GI

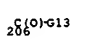


AB The title compds. I [A = (un)substituted benzene, etc.; X, Y = (O- or N-containing) alkylene; Z = amino, OH, carboxyl, aminocarbonyl, etc.] are prepared The title compds. in vitro showed IC50 values of 0.068 to 15.3 μM against thrombin-induced platelet aggregation.

MSTR 1



G1 = biphenylyl (opt. substd. by 1 or more G2)
G9 = NH (opt. substd.)
G10 = phenylene
G11 = alkylene <containing 1-5 C>
G12 = 206



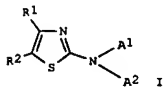
G13 = OH
Derivative: and medically acceptable salts
Patent location: claim 1
Note: G8 alkylene may be interrupted by oxygen or nitrogen

L6 ANSWER 43 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)

L6 ANSWER 44 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 125:123706 MARPAT
TITLE: Antibacterial or bactericide comprising 2-aminothiazole derivative and salts thereof
INVENTOR(S): Hashiguchi, Terushi; Yoshida, Toshio; Itoyama, Toshio;
Taniguchi, Yasuaki
PATENT ASSIGNEE(S): Hisamitsu Pharmaceutical Co., Inc., Japan
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9616650	A1	19960606	WO 1995-JP2347	19951116
W: AU, CA, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2206315	AA	19960606	CA 1995-2206315	19951116
AU 9538809	A1	19960619	AU 1995-38809	19951116
AU 689972	B2	19980409		
EP 790057	A1	19970820	EP 1995-938022	19951116
EP 790057	B1	20020605		
R: CH, DE, FR, GB, IE, LI				
JP 3023178	B2	20000321	JP 1996-518570	19951116
TW 414708	B	20001211	TW 1995-84112972	19951206
US 5856347	A	19990105	US 1997-836924	19970523

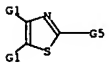
PRIORITY APPLN. INFO.: JP 1994-317737 19941129
JP 1994-335388 19941222
WO 1995-JP2347 19951116
GI



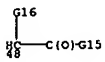
AB An antibacterial or bactericide comprising a 2-aminothiazole derivative represented by general formula (I) or a salt thereof, wherein R1 and R2 represent each hydrogen, halogeno, lower alkyl, lower cycloalkyl (un)substituted Ph, thiophene, benzoyl, benzoylmethyl, optionally substituted benzyl, p-pivoloyloxyphenyl, -COOR3 (wherein R3 represents hydrogen or lower alkyl) or -CH2COOR4 (wherein R4 represents hydrogen, lower alkyl or optionally substituted benzyl); and A1 and A2 represent each hydrogen, lower alkanesulfonyl, halogenated lower alkanesulfonyl, optionally substituted Ph, substituted benzoyl, substituted benzyl, (un)substituted benzenesulfonyl, (un)substituted lower alkanoyl, amidino, -CO-R5 wherein R5 represents lower alkyl, optionally substituted Ph, -(CH2)m-COOH (wherein m represents an integer of 1 to 5), -(CH2)n-NH-R6 (wherein n represents an integer of 1 to 5, and R6 represents hydrogen, tert-butoxycarbonyl or benzyloxycarbonyl) or -(CH2)Q-R7 (wherein Q represents an integer of 0 to 5, and R7 represents lower alkoxy, optionally substituted Ph, optionally substituted pyridyl or cyclic

L6 ANSWER 44 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
amino), or A1 and A2 are combined with each other to represent cyclic amino.

MSTR 1



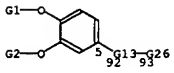
G2 = Ph / 48



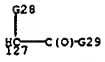
G5 = 31

G6 = Ph (opt. substd. by (1-3) G2)
G15 = OH (opt. substd.)
Derivative: or salts
Patent location: claim 1

L6 ANSWER 45 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)



G21 = NH
G23 = phenylene (opt. substd. by (1) G15)
G27 = 127

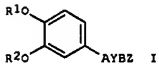


G29 = OH
G38 = phenylene
Derivative: and pharmaceutically acceptable salts
Patent location: claim 1
Note: substitution is restricted
Stereochemistry: racemic-diastereomeric mixtures and optical isomers

L6 ANSWER 45 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 125:58532 MARPAT
TITLE: Preparation of catechol diethers as inhibitors of tumor necrosis factor release.
INVENTOR(S): Cohan, Victoria L.; Duplantier, Allen J.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Eur. Pat. Appl., 35 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 706795	A2	19960417	EP 1995-306159	19950904
EP 706795	A3	19971217		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
TW 492862	B	20020701	TW 1995-84108419	19950812
IL 115311	A1	20000229	IL 1995-115311	19950914
CA 2158632	AA	19960322	CA 1995-2158632	19950919
CA 2158632	C	19980602		
CN 1129102	A	19960821	CN 1995-117355	19950919
AU 9531772	A1	19960404	AU 1995-31772	19950920
JP 08134073	A2	19960528	JP 1995-241698	19950920
ZA 9507925	A	19970320	ZA 1995-7925	19950920
PRIORITY APPLN. INFO.:			US 1994-310171	19940921

GI



AB Use of title compds. [I; R1 = Me, Et, F2CH, CF3; R2 =(substituted) alkyl, alkoxyalkyl, phenoxyalkyl, cycloalkyl, polycycloalkyl, phenylaminoalkyl; A, B = bond, (substituted) alkylene, alkenyl, phenylene; Y = bond, O, imino, S; Z = (substituted) imidazolyl, pyridyl, Ph, etc.; with provisos] for inhibiting production of TNF is claimed (no data). I are useful in the treatment or alleviation of inflammatory conditions, sepsis, septic shock, tuberculosis, graft vs. host disease, multiple sclerosis and other autoimmune diseases, and cachexia associated with AIDS or cancer. Thus, 3-exo-norbornyloxy-4-methoxyacetophenone and glyoxylic acid were heated at 120° for 2.2 h. The melt was cooled to 60° and treated with H2O, aqueous NH3, and N2H4 to give 49% 6-[3-(bicyclo[2,2,1]hept-2-yloxy)-4-methoxyphenyl]-3(2H)-pyridazinone.

MSTR 1A

L6 ANSWER 46 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 124:76527 MARPAT
TITLE: Treatment of atherosclerosis with angiotensin II receptor blocking imidazoles
INVENTOR(S): Nelson, Edward B.; Sweet, Charles S.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9526188	A1	19951005	WO 1995-US3700	19950324
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2186606	AA	19951005	CA 1995-2186606	19950324
AU 9521279	A1	19951017	AU 1995-21279	19950324
AU 696868	B2	19980917		
EP 754042	A1	19970122	EP 1995-914177	19950324
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 09510973	T2	19971104	JP 1995-525233	19950324
US 5663186	A	19970902	US 1995-466483	19950606
US 5663187	A	19970902	US 1995-466484	19950606
PRIORITY APPLN. INFO.:			US 1994-219685	19940329
			WO 1995-US3700	19950324

AB A method of treatment for atherosclerosis and/or reducing cholesterol using an angiotensin II antagonist. This method of treatment can be used in conjunction with the treatment of hypertension. Substituted imidazoles are useful as angiotensin II receptor antagonists for this method of treatment. A method of treatment for atherosclerosis and/or reducing cholesterol using an angiotensin II receptor antagonist in combination with an HMG-CoA reductase inhibitor is described. Pharmaceutical compns. of the compds. are described. The effectiveness of the imidazoles in inhibiting atherosclerosis was demonstrated in rats.

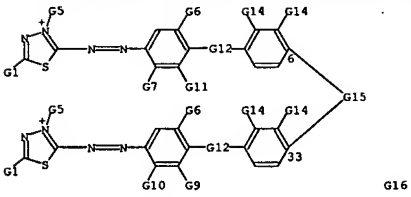
MSTR 1

G1 = phenylene (opt. substd.)
G9 = NH (opt. substd.)
G10 = phenylene (opt. substd.)
G26 = CH2CO2H
G27 = 320-5 321-1 318-4 319-3

L6 ANSWER 46 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)

Derivative: and pharmaceutically acceptable salts
Patent location: claim 2
Note: substitution is restricted

L6 ANSWER 47 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)



G11 = alkyl (opt. substd. by G17)
G12 = NH
G15 = 127

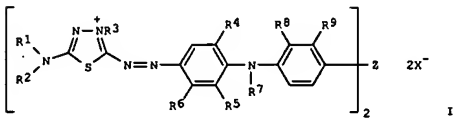
G17 = CO2H
Patent location: claim 1

L6 ANSWER 47 OF 59 MARPAT COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 124:10882 MARPAT
TITLE: Cationic thiadiazole dyes, their preparation and their use
INVENTOR(S): Berneth, Horst; Claussen, Uwe; Hartwich, Werner; Wild, Peter
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 675169	A2	19951004	EP 1995-103945	19950317
EP 675169	A3	19960612		
EP 675169	B1	19980916		
R: CH, DE, FR, GB, LI, SE				
DE 4411065	A1	19951005	DE 1994-4411065	19940330
US 5580964	A	19961203	US 1995-409374	19950323
JP 07268226	A2	19951017	JP 1995-90117	19950324
PRIORITY APPLN. INFO.:			DE 1994-4411065	19940330

GI



AB The dyes (I; R1, R2 = H, organic group; R1R2N = heterocyclic group; R3 = hydrocarbyl; R4, R5 = H, alkyl, alkoxy, halogen; R6 = H, organic group, halogen, CN, NO2; R5R6 = CH:CHCH:CH; R7 = H, hydrocarbyl; R8, R9 = H, alkyl, alkoxy, halogen; Z = divalent group; X- = anion) are obtained by coupling of diazotized 2-aminothiadiazoles with diphenylamine derivs. followed by quaternization. I have good fastness properties and may be used for dyeing and printing of textiles and paper and as dichroic dyes in polarizer films. Thus, 3,4-dimethoxyaniline was acetylated and treated with 2-amino-5-[bis(2-hydroxypropyl)amino]-1,3,4-thiadiazole and the product was methylated, diazotized, and coupled with 4,4'-iminodianiline to give a dye (λmax 645), light greenish blue on paper.

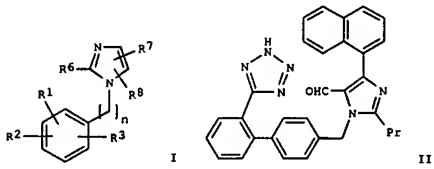
MSTR 1

L6 ANSWER 48 OF 59 MARPAT COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 123:286029 MARPAT
TITLE: Preparation of N-aralkylimidazoles as angiotensin II antagonists
PATENT ASSIGNEE(S): du Pont de Nemours, E. I., and Co., USA
SOURCE: Israeli, 199 pp.
CODEN: ISXXAQ
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

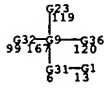
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IL 95259	A1	19950315	IL 1990-95259	19900801
PRIORITY APPLN. INFO.:			IL 1990-95259	19900801

GI



AB Title compds. [I; R1 = CO2H, tetrazolyl, SO3H, carboxyphenyl, etc.; R2 = H, halo, cyano, alkyl, alkoxy, etc.; H, halo, alkyl, alkoxy; R6 = (cyclo)alk(en)yl, CH2Ph, etc.; R7 = naphthyl, quinolyl, indolyl, etc.; R8 = tetrazolylalkyl, hydroxyalkyl, alkanoyl, etc.; n = 0-2] were prepared Thus, 4-iodo-2-propylimidazole-5-carboxaldehyde (preparation given) was condensed with 1-naphthylboronic acid and the product N-alkylated by 4-bromomethyl-2'-(N-triphenylmethyl-1H-tetrazol-5-yl)biphenyl (preparation given) to give, after deprotection, title compound II which had IC50 of 0.021μM against angiotensin II binding at rat adrenal cortical microsomes in vitro and gave significant (sic) decrease in blood pressure in renal hypertensive rats at 30mg/kg oraly.

MSTR 1



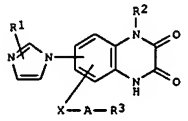
L6 ANSWER 48 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
G9 = 3-6 4-99 1-119 2-120

G11 = CH2CO2H
G12 = NH (opt. substd.)
G13 = phenylene (opt. substd.)
G31 = p-C6H4 (opt. substd.)
Derivative: or pharmaceutically acceptable salts
Patent location: claim 1
Note: substitution is restricted
Note: incorporates claim 54

L6 ANSWER 49 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 122:314573 MARPAT
TITLE: Preparation of imidazolylquinoxalinedione derivatives as glutamate receptor antagonists
INVENTOR(S): Sakamoto, Shuichi; Shishikura, Jun-ichi; Iwata, Masahiro; Okada, Masamichi; Sasamata, Masao
PATENT ASSIGNEE(S): Yamparm, Japan
SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9426737	A1	19941124	WO 1994-JP758	19940511
W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KG, KR, KZ, LK, LV, MD, MG, MN, MW, NO, NZ, PL, PT, RO, RU, SD, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9466903	A1	19941212	AU 1994-66903	19940511
PRIORITY APPLN. INFO.:			JP 1993-134033	19930512
			JP 1993-296525	19931126
			WO 1994-JP758	19940511

GI

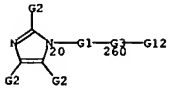


I

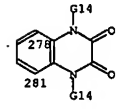
AB Title compds. I [R1 = H, alkyl; R2 = H, OH; X = O, NR4, S(O)m; R3 = alkyl, carboxy, or (un)substituted Ph, cycloalkyl or mono- or bicyclic heterocyclic group; R4 = H, alkyl; n = 0, 1, 2; A = direct bond, alkylene] and their pharmaceutically acceptable salts, useful as glutamate receptor antagonists, psychotropics, nerve cell protecting agents, and for treatment of brain ischemia, were prepared Thus, reduction of 5-(1H-imidazol-1-yl)-4-methoxy-2-nitroaniline with H in MeOH in the presence of PtO2 and HCl at room temp for 2.5 h followed by cyclocondensation with oxalic acid in aqueous HCl gave 6-(1H-imidazol-1-yl)-7-methoxyquinoxaline-2,3(1H,4H)-dione hydrochloride. 4-{[4-Hydroxy-7-(1H-imidazol-1-yl)-2,3-dioxo-1,2,3,4-tetrahydroquinoxalin-6-yl]oxymethyl}benzoic acid hydrochloride showed nerve cell protection activity in mice.

L6 ANSWER 49 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)

MSTR 1



G1 = 278-20 281-260

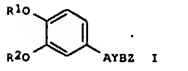


G3 = NH
G7 = alkyl <containing 1-6 C> (substd. by CO2H)
G12 = Ph (opt. substd. by 1 or more G7)
Derivative: or pharmaceutically acceptable salts
Patent location: claim 1

L6 ANSWER 50 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 121:255405 MARPAT
TITLE: Catechol diethers as selective phosphodiesterase IV inhibitors
INVENTOR(S): Duplantier, Allen J.; Eggler, James F.; Marfat, Anthony; Masamune, Hiroko
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: PCT Int. Appl., 159 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9412461	A1	19940609	WO 1993-US10228	19931029
W: AU, BR, CA, CZ, JP, KR, NO, NZ, PL, RU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2150812	AA	19940609	CA 1993-2150812	19931029
CA 2150812	C	20021224		
CA 2400368	AA	19940609	CA 1993-2400368	19931029
AU 9455396	A1	19940622	AU 1994-55396	19931029
AU 673569	B2	19961114		
EP 672031	A1	19950920	EP 1994-900390	19931029
EP 672031	B1	20030312		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 08501318	T2	19960213	JP 1994-513129	19931029
JP 3100984	B2	20001023		
BR 9307570	A	19990525	BR 1993-7570	19931029
AT 234270	E	20030315	AT 1994-900390	19931029
PT 672031	T	20030630	PT 1994-900390	19931029
ES 2192192	T3	20031001	ES 1994-900390	19931029
IL 107758	A1	19971120	IL 1993-107758	19931125
FI 9305379	A	19940603	FI 1993-5379	19931201
ZA 9308978	A	19950601	ZA 1993-8978	19931201
HU 65928	A2	19940728	HU 1993-3423	19931202
CN 1094028	A	19941026	CN 1993-112776	19931202
NO 9502178	A	19950801	NO 1995-2178	19950601
US 5814651	A	19980929	US 1997-872686	19970610
PRIORITY APPLN. INFO.:			US 1992-984408	19921202
			CA 1993-2150812	19931029
			WO 1993-US10228	19931029
			US 1993-142328	19931126

GI

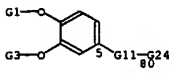


AYBZ I

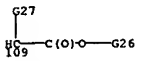
AB The title compds. [I; A, B = direct bond, (un)substituted C1-5 alkylene, (un)substituted alkenyl, (un)substituted phenylene; R1 = Me, Et, CF2H, CF3; R2 = C1-6 alkyl, alkoxyalkyl, phenoxyalkyl, cycloalkyl, etc.; Y = direct bond, O, NR6, S; R6 = H, C1-4 alkyl; Z = (un)substituted monocyclic

L6 ANSWER 50 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
or bicyclic heterocyclyl], which are inhibitors of phosphodiesterase IV (no data), useful in the treatment of inflammatory conditions (no data), etc., are prepd. Thus, 3-(carbomethoxy)benzyltriphenylphosphonium bromide was reacted with 3-cyclopentyloxy-4-methoxybenzaldehyde in the presence of BuLi, producing Me 3-[2-[3-(cyclopentyloxy)-4-methoxyphenyl]ethenyl]benzoate (36% cis-isomer, 36% trans-isomer).

MSTR 1



G14 = phenylene (opt. substd. by (1) G12)
G18 = NH
G24 = Ph (opt. substd. by (1-5) G25)
G25 = 109

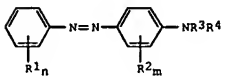


Derivative: and pharmaceutically acceptable salts
Patent location: claim 1
Note: substitution is restricted
Stereochemistry: racemic-diastereomeric mixtures and optical isomers

L6 ANSWER 51 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 119:282353 MARPAT
TITLE: Optical recording media containing laser beam-sensitive 4-aminoazobenzenes
INVENTOR(S): Nakamura, Yoshinori; Eguchi, Hiroshi
PATENT ASSIGNEE(S): Dai Nippon Printing Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

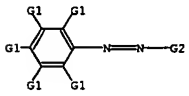
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 05193263	A2	19930803	JP 1992-27508	19920120

PRIORITY APPLN. INFO.: JP 1992-27508 19920120
GI



AB Optical recording media comprising a substrate and a recording layer containing the title compds. I [R1-2 = H, halo, NO2, cyano, OH, (un)substituted alkyl, cycloalkyl, allyl, aryl, vinyl, aralkyl, heterocyclyl, alkoxy, OPh, alkylthio, arylthio, alkoxyalkyl, aralkylalkoxyalkyl, CONH2, SO2NH2, oxycarbonylalkyl, oxycarbonyl, carboxyalkyl, carbonylamino, sulfonylamino, NH2, CO2H, ureido; R3-4 = H, halo, (un)substituted alkyl, cycloalkyl, allyl, aryl, vinyl, aralkyl, heterocyclyl, alkoxyalkyl, aralkylalkoxyalkyl, oxycarbonylalkyl, carboxyalkyl, hydroxyalkyl; m, n = 1-5; R3 and R4 or R2 may be bonded together to form a ring] as light-absorbing substances is claimed. The optical recording medium show high sensitivity to laser beam and are excellent in storage stability.

MSTR 1



G2 = 10

L6 ANSWER 51 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)

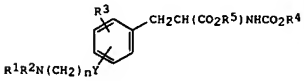
G3 = alkyl (substd. by CO2H (opt. substd.))
G4 = 39

G7 = biphenylyl
Patent location: claim 1

L6 ANSWER 52 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 119:138886 MARPAT
TITLE: Preparation of aminoalkyl-substituted phenylpropionic acid derivatives for inhibiting osteoclast-mediated bone resorption.
INVENTOR(S): Egbertson, Melissa S.; Gould, Robert J.; Hartman, George D.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 52 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

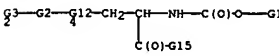
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 528586	A1	19930224	EP 1992-307156	19920805
EP 528586	B1	19950222		
R: CH, DE, FR, GB, IT, LI, NL				
US 5217994	A	19930608	US 1991-743475	19910809
CA 2088518	AA	19930210	CA 1992-2088518	19920807
JP 06056662	A2	19940301	JP 1992-212981	19920810
JP 07047536	B4	19950524		

PRIORITY APPLN. INFO.: US 1991-743475 19910809
GI



AB Title compds. I (n = 0-6; Y = H2C, O, SO2, CONH, NHCO, CO; R1, R2 = H, C1-8 (substituted) alkyl, -arylalkyl, -aminoalkyl, -heterocyclylalkyl, etc.; R3 = H, C1-6 alkyl, halo, F3C, etc.; R4 = C1-6 alkyl, arylalkyl, heterocyclylalkyl; R5 = H, C1-6 alkyl, arylalkyl, C1-6 alkylcarbonyloxymethyl) and a salt thereof, showing bone resorption inhibition, are prepared N-CBZ-tyrosine in DMF was treated with BrCH2CH2CH2Cl to give 2-S-(N-benzyloxycarbonylamino)-3-[4-(3-chloropropoxy)phenyl]propionic acid (II). Treatment of N-BOC-L-tyrosine with NaH in DMF followed by BrCH2CH2CH2Cl provided the N-BOC analog of II which was reacted with Me3CNH2 in refluxing MeCN for 2 days to give S-I (R1R2 = Me3C, n = 3; Y = O, R3 = R5 = H, R4 = Ph).

MSTR 1A



G3 = 18

L6 ANSWER 52 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)

G4 = Ph (opt. substd. by 1 or more G5)
G5 = Ph
G6 = carbon chain <containing 1-4 C, 0 or more double bonds, 0 or more triple bonds>
G7 = CO2H
Generic group attributes: 67 69 76 <containing 1-4 C, 0 or more double bonds, 0 or more triple bonds>
Derivative: and pharmaceutically acceptable salts
Patent location: claim 1

L6 ANSWER 53 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 118:38918 MARPAT
TITLE: Preparation of thiazolidine-2,4-dione derivatives as hypoglycemic agents and aldose reductase inhibitors
INVENTOR(S): Ohnota, Michiro; Murakami, Koji; Okamura, Kyuya; Hirata, Yoshihiro; Ohashi, Mitsuo
PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9214730	A1	19920903	WO 1992-JP190	19920224
W: AU, CA, HU, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
JP 04270273	A2	19920925	JP 1991-53278	19910225
CA 2081112	AA	19920826	CA 1992-2081112	19920224
AU 9212460	A1	19920915	AU 1992-12460	19920224
AU 645177	B2	19940106		
EP 527232	A1	19930217	EP 1992-905306	19920224
EP 527232	B1	19980923		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
HU 67173	A2	19950228	HU 1992-3293	19920224
HU 218662	B	20001028		
AT 171450	E	19981015	AT 1992-905306	19920224
ES 2123549	T3	19990116	ES 1992-905306	19920224
US 5308856	A	19940503	US 1992-938228	19921026
PRIORITY APPLN. INFO.:			JP 1991-53278	19910225
			WO 1992-JP190	19920224

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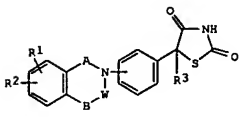
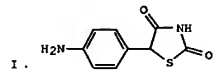
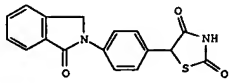


I



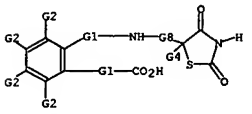
II



III

L6 ANSWER 53 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
AB The title compds. [I; R1,R2 = H, halo, alkyl, alkoxy, OH, (substituted) NH2, NO2; R3 = H, alkyl; A = alkylene, CO; B, W = alkylene, CO, bond, but B = W] are prepared A solution of 4.90 g aniline derivative II and 3.54 g phthalaldehydic acid in EtOH was refluxed, cooled, and stirred with 1.78 g NaBH4 to give 6.90 g III, which showed hypoglycemic activity at 10 mg/kg orally in mice.

MSTR 4



G1 = (0-2) CH2
G8 = phenylene
Patent location: claim 2

L6 ANSWER 54 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 117:157638 MARPAT
TITLE: Treatment of cardiac and vascular hypertrophy and hyperplasia with angiotensin II receptor blockers
INVENTOR(S): Heitsch, Holger; Henning, Rainer; Linz, Wolfgang; Schoelkens, Bernward; Urbach, Hansjoerg
PATENT ASSIGNEE(S): Hoechst A.-G., Germany
SOURCE: Ger. Offen., 20 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4036706	A1	19920521	DE 1990-4036706	19901117
EP 492105	A2	19920701	EP 1991-119183	19911111
EP 492105	A3	19920729		
EP 492105	B1	19940720		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ES 2060274	T3	19941116	ES 1991-119183	19911111
BR 9104918	A	19920623	BR 1991-4918	19911113
US 5236943	A	19930817	US 1991-791501	19911114
CA 2055637	AA	19920518	CA 1991-2055637	19911115
CA 2055637	C	20031111		
NO 9104482	A	19920518	NO 1991-4482	19911115
AU 9187858	A1	19920521	AU 1991-87858	19911115
AU 652590	B2	19940901		
HU 59599	A2	19920629	HU 1991-3581	19911115
HU 219404	B	20010428		
ZA 9109056	A	19920729	ZA 1991-9056	19911115
JP 04290823	A2	19921015	JP 1991-326663	19911115
JP 3370347	B2	20030127		
CZ 283236	B6	19980218	CZ 1991-3471	19911115
KR 221686	B1	19990915	KR 1991-20342	19911115
SK 280304	B6	19991108	SK 1991-3471	19911115
CN 1062289	A	19920701	CN 1991-110817	19911116
CN 1049116	B	20000209		
HR 940765	B1	20000831	HR 1994-940765	19941025
PRIORITY APPLN. INFO.:			DE 1990-4036706	19901117
			YU 1991-1854	19911125

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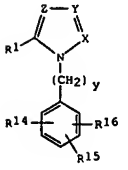
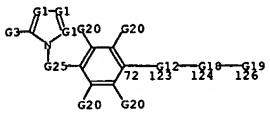


I

L6 ANSWER 54 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)

AB The title receptor blockers (I; X, Y, Z = N, CR2; R1 = alkyl, alkenyl, alkynyl, cycloalkyl, alkoxy, etc.; R2 = H, halo, nitro, cyano, Ph, etc.; R14 = 4-CO2H, SO3H, PO3H2, SO2NH2, etc.; R15 = H, halo, nitro, cyano, alkyl, alkoxy, acyloxy, etc.; R16 = H, halo, nitro, cyano, alkyl, alkoxy, aryl, furyl, tetrazolyl; y = 0-2) are useful for treatment of cardiac and vascular hypertrophy and hyperplasia. Thus, tablets were prepared containing 2-butyl-4-chloro-5-hydroxymethyl-1[[[2'-(1H)-tetrazol-5-yl]biphenyl-4-yl]methyl]imidazole K salt 20.0, corn starch 140.0, gelatin 7.5, microcryst. cellulose 2.5, and Mg stearate 2.5 g/1000 tablets for oral administration.

MSTR 1B



G1 = N
G12 = NH (opt. substd.)
G18 = phenylene (opt. substd.)
G19 = CH2CO2H
Derivative: or physiologically acceptable salts
Patent location: claim 2

L6 ANSWER 55 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 116:166252 MARPAT
TITLE: Treatment of chronic renal failure with imidazole angiotensin II receptor antagonists
INVENTOR(S): Carini, David John; Duncia, John Jonas Vytautas; Wong,
Pancras Chor Bun
PATENT ASSIGNEE(S): du Pont de Nemours, E. I., and Co., USA
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

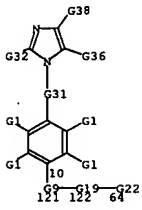
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9200067	A2	19920109	WO 1991-US3906	19910607
WO 9200067	A3	19930527		
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
CA 2085584	AA	19911223	CA 1991-2085584	19910607
CA 2085584	C	20030211		
EP 533840	A1	19930331	EP 1991-912884	19910607
EP 533840	B1	19961211		
R: AT, BE, CH, DE, DK, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05509086	T2	19931216	JP 1991-512070	19910607
AT 146076	E	19961215	AT 1991-912884	19910607
JP 11228410	A2	19990824	JP 1998-321761	19910607
US 5210079	A	19930511	US 1992-832638	19920207

PRIORITY APPLN. INFO.: US 1990-542351 19900622
US 1988-142580 19880107
US 1988-279194 19881206
US 1989-373755 19890630
JP 1991-512070 19910607
WO 1991-US3906 19910607

AB Chronic renal failure mediated by angiotensin II is treated with substituted imidazoles such as 2-butyl-4-chloro-1-[(2'-(1H-tetrazol-5-yl)biphenyl-4-yl)methyl]-5-(hydroxymethyl)imidazole and 2-butyl-4-chloro-1-[(2'-carboxybiphenyl-4-yl)methyl]-5-(hydroxymethyl)imidazole and pharmaceutically acceptable salts thereof.

MSTR 1D

L6 ANSWER 55 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)



G9 = 123

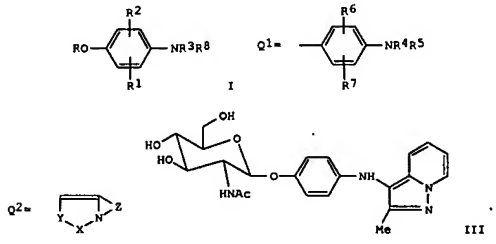
G19 = phenylene (opt. substd.)
G22 = CH2CO2H
Derivative: or pharmaceutically acceptable salts
Patent location: claim 1
Note: substitution is restricted

L6 ANSWER 56 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 116:152291 MARPAT
TITLE: Preparation of N- and O-substituted aminophenols as hydrolase substrates
INVENTOR(S): Mangold, Dieter; Zimmermann, Gerd
PATENT ASSIGNEE(S): Boehringer Mannheim G.m.b.H., Germany
SOURCE: Eur. Pat. Appl., 64 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 433855	A2	19910626	EP 1990-123836	19901211
EP 433855	A3	19950322		
EP 433855	B1	20010307		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DE 3942355	A1	19910627	DE 1989-3942355	19891221
AT 199559	E	20010315	AT 1990-123836	19901211
ES 2156105	T3	20010616	ES 1990-123836	19901211
JP 04305593	A2	19921028	JP 1990-413426	19901221
JP 2534401	B2	19960918		
US 5334505	A	19940802	US 1990-633231	19901221
US 5525480	A	19960611	US 1994-257688	19940609
JP 07179463	A2	19950718	JP 1994-240024	19941004

PRIORITY APPLN. INFO.: DE 1989-3942355 19891221
US 1990-633231 19901221

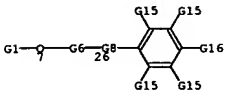
GI



AB N- And O-substituted aminophenols I (R = glycoside residue, acyl, PO3H2, SO3H, etc.; R1, R2 = H, halo, SO3H, PO3H2, OH, NO2, CO2H, etc.; R3 = H, COCO2H, SO3H, (substituted) alkenoyl or aryloyl, etc.; R8 = Q1, Q2; R4, R5 = alkyl, or NR4R5 = (substituted) 3-6 membered saturated heterocyclyl containing O, S, or N; R6, R7 = H, halo, OH, carboxamido, (substituted) alkyl, etc.; XY = NR9CO, N:COR10; R9 = H, alkyl; R10 = (substituted) alkyl, alkenyl, or

L6 ANSWER 56 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
alkynyl, etc.; Z = 3-5 membered hydrocarbon chain which may contain N and/or S atom(s), etc.; with provisos], useful as hydrolase substrates, were prepd. Thus, 3-acetyl-2-methylpyrazolo[1,5-a]pyridine was converted to the 3-nitroso compd. by NaNO2 in 6N HCl. This was reduced by SnCl2 to the corresponding amine hydrochloride, which was coupled with PhOH in pyridine to give (4-hydroxyphenyl)-(2-methylpyrazolo[1,5-a]pyridin-3-yl)amine (II). Condensation of II with 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-α-D-glucosyl chloride gave title compd. III. A calibration curve for detn. of N-acetyl-β-D-glucosaminidase (IV) by III was made with λmax of 560 nm. III changes from colorless to blue-violet in the presence of IV.

MSTR 1A



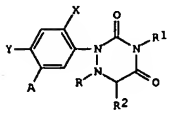
G2 = alkyl <containing 1-6 C>
(opt. substd. by 1 or more G12)
G6 = 6-7 3-26 / 6-26 3-7

G8 = NH
G12 = CO2H
G16 = morpholino
Derivative: or salts
Patent location: claim 1
Note: substitution is restricted

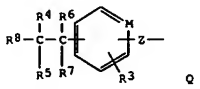
L6 ANSWER 57 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 114:81892 MARPAT
TITLE: Preparation of herbicidal triazinediones
INVENTOR(S): Theodoridis, George
PATENT ASSIGNEE(S): FMC Corp., USA
SOURCE: U.S., 10 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4956004	A	19900911	US 1989-350053	19890510

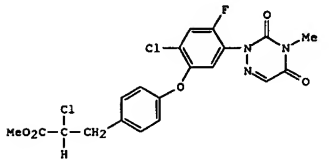
PRIORITY APPLN. INFO.: US 1989-350053 19890510
GI



I



Q

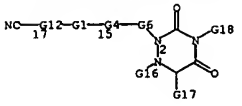


II

AB Title compds. I [R1 = (halo)alkyl; R, R2 = H, or RR2 = bond; X = H, halo, (halo)alkyl, NO2; Y = H, halo, alkyl(thio), (halo)alkyl, (halo)alkoxy, SOCF3; A = Q; R3 = H, halo, (halo)alkyl, NO2, NH2, alkoxy, alkylthio, cyano; R4 = H, halo, alkyl, alkenyl, alkynyl; R5 = H, halo, alkyl, alkenyl, alkynyl, cyano, R8; R6 = H, halo, alkyl, alkoxy; or R5R6 = bond; R7 = H, alkyl; R8 = CHO, CO2H and salts, alkoxycarbonyl, cyano, etc.; Z = O, S, NH, alkylimino; M = CH, N], useful as herbicides (no data), are prepared For example, II is prepared in 3 steps from 2-(4-chloro-2-fluoro-5-hydroxyphenyl)-4-methyl-1,2,4-triazine-3,5(2H,4H)-dione.

MSTR 2A

L6 ANSWER 57 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)



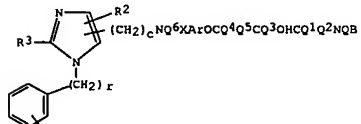
G1 = phenylene (opt. substd. by 1 or more G2)
G4 = NH
G6 = p-C6H4 (opt. substd.)
G7 = OH
G12 = carbon chain <containing 2 or more C>
(opt. substd. by 1 or more G13)
G14 = 43

Patent location: disclosure

L6 ANSWER 58 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 113:115303 MARPAT
TITLE: Arylinidazoles as combination β-blocking/angiotensin II blocking antihypertensives
INVENTOR(S): Carini, David J.; Duncia, John J. V.
PATENT ASSIGNEE(S): du Pont de Nemours, E. I., and Co., USA
SOURCE: U.S., 13 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4916129	A	19900410	US 1989-299709	19890119
CA 2006604	AA	19900719	CA 1989-2006604	19891222
EP 380959	A1	19900808	EP 1990-100874	19900117
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL				
NO 9000264	A	19900720	NO 1990-264	19900118
HU 53618	A2	19901128	HU 1990-184	19900118
HU 205352	B	19920428		
JP 03002169	A2	19910108	JP 1990-7287	19900118
AU 9048545	A1	19900726	AU 1990-48545	19900119
AU 618503	B2	19911219		
ZA 9000402	A	19910925	ZA 1990-402	19900119

PRIORITY APPLN. INFO.: US 1989-299709 19890119
OTHER SOURCE(S): CASREACT 113:115303
GI



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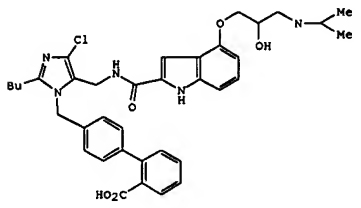
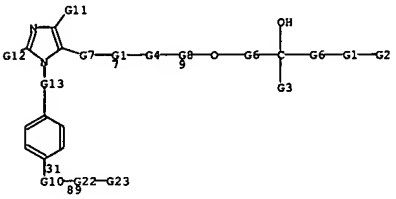


II

L6 ANSWER 58 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)

AB The title compds. [I; Q-Q6 = H, alkyl; X = CO, CONH, CO2; B = alkyl; Ar = (substituted) phenylene, naphthylene, indolylene; R1 = carboxylate (esters), tetrazolyl, (substituted) Ph, furyl, thienyl, NHSO2CF3, CONHOH, etc.; R2 = H, F, Cl, Br, I, NO2, (perfluoro)alkyl, Ph, cyano, etc.; R3 = alkyl, alkenyl, alkynyl, alkylthio; c = 1-10; r = 0-2], having both β-adrenoceptor and angiotensin converting enzyme inhibiting activities, were prepared Thus, title compound II was prepared from 5-aminomethyl-2-n-butyl-1-[(2'-carbomethoxybiphenyl-4-yl)methyl]-4-chloroimidazole and 4-[3-(N-tert-butoxycarbonyl-N-isopropylamino)-2-hydroxypropoxy]indole-2-carboxylic acid in DMF containing DCC and 1-hydroxybenzotriazole at 0°. II at 3 mg/kg i.v. in pithed rats shifted the dose-tachycardic response curve for isoproterenol toward approx. 10-fold higher dose values.

MSTR 1B



G10 = NH
G22 = phenylene (opt. substd.)
G23 = CH2CO2H
Derivative: or pharmaceutically acceptable salts
Patent location: claim 1

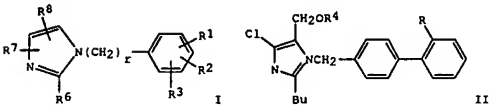
L6 ANSWER 59 OF 59 MARPAT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 112:118817 MARPAT
TITLE: Preparation of (biphenylylmethyl)imidazoles and analogs as antihypertensive agents
INVENTOR(S): Carini, David John; Wong, Pancras Chor Bun; Duncia, John Jonas Vytautas
PATENT ASSIGNEE(S): du Pont de Nemours, E. I., and Co., USA
SOURCE: Eur. Pat. Appl., 271 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 324377	A2	19890719	EP 1989-100144	19890105
EP 324377	A3	19910206		
EP 324377	B1	19970416		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5138069	A	19920811	US 1988-279194	19881206
CA 1338238	A1	19960409	CA 1988-586904	19881222
WO 8906233	A1	19890713	WO 1989-US52	19890105
W: JP				
JP 03501020	T2	19910307	JP 1989-501656	19890105
JP 07025738	B4	19950322		
EP 733366	A2	19960925	EP 1996-107930	19890105
EP 733366	A3	19961009		
EP 733366	B1	19980401		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 151755	E	19970515	AT 1989-100144	19890105
ES 2100150	T3	19970616	ES 1989-100144	19890105
AT 164520	E	19980415	AT 1996-107930	19890105
ES 2117463	T3	19980801	ES 1996-107930	19890105
DK 8900051	A	19890708	DK 1989-51	19890106
DK 174948	B1	20040315		
FI 8900070	A	19890708	FI 1989-70	19890106
FI 99012	B	19970613		
FI 99012	C	19970925		
NO 8900075	A	19890710	NO 1989-75	19890106
NO 177265	B	19950508		
NO 177265	C	19950816		
AU 8927771	A1	19890713	AU 1989-27771	19890106
AU 617736	B2	19911205		
ZA 8900127	A	19900926	ZA 1989-127	19890106
SU 1814646	A3	19930507	SU 1989-4613475	19890106
HU 64038	A2	19931129	HU 1989-50	19890106
HU 218201	B	20000628		
US 5128355	A	19920707	US 1989-435869	19891113
US 5153197	A	19921006	US 1989-436165	19891113
US 5155118	A	19921013	US 1989-436281	19891113
RU 2017733	C1	19940815	RU 1992-5010637	19920127
US 5210079	A	19930511	US 1992-832638	19920207
US 5354867	A	19941011	US 1993-47883	19930415
PRIORITY APPLN. INFO.:			US 1988-142580	19880107
			US 1988-279194	19881206

L6 ANSWER 59 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)

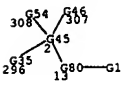
	US 1986-884920	19860711
	US 1987-50341	19870522
	EP 1989-100144	19890105
	WO 1989-US52	19890105
	US 1989-373755	19890630
	US 1990-542351	19900622
	US 1990-545240	19900627

GI



AB The title compds. [I; R1 = acyl, tetrazolyl, aminoacyl, acylamino, biphenylyl, etc.; R2 = H, halo, NO2, cyano, C1-4 alkyl, etc.; R3 = H, halo, C1-4 alkyl, alkoxy; R6 = C2-10 alkyl, C3-10 alkenyl, alkynyl, C3-8 cycloalkyl, (un)substituted Ph, PhCH2, etc.; R7 = H, halo, NO2, cyano, pentafluorophenyl, etc.; R8 = H, cyano, C1-10 (fluoro)alkyl, etc.; r = 0-2] were prepared Thus, 2-butyl-4-chloro-5-hydroxymethylimidazole was stirred 0.5 h with NaOMe in MeOH and the product stirred overnight with 4'-bromomethyl-2-cyanobiphenyl (preparation given) in DMF to give title compound II (R = cyano, R4 = H) which was converted in 2 steps to II (R = cyano, R4 = Me). The latter was stirred 2 days at 100° and 11 days at 120° with NaN3 in DMF containing NH4Cl to give II (R = 1H-tetrazol-5-yl, R4 = Me) the Na salt of which had IC50 of 0.020 μM for inhibition of angiotensin II receptor binding and showed significant decreases in blood pressure in rats at ≤10 and ≤100 mg/kg i.v. and orally, resp.

MSTR 1



G10 = NH (opt. substd.)
G18 = 103

G19 = CO2H (opt. substd.)

L6 ANSWER 59 OF 59 MARPAT COPYRIGHT 2005 ACS on STN (Continued)
G24 = 95-65 94-102

G31 = p-C6H4 (opt. substd.)
G45 = 309-296 3-13 5-308 4-307

Derivative: and pharmaceutically acceptable salts
Patent location: claim 1
Note: substitution is restricted

```
=> file reg

=> s l7 full
L9          626 SEA SSS FUL L7

=> s l8 full
L10         580 SEA SSS FUL L8

=> s l9 not l10
L11          46 L9 NOT L10

=> file ca


=> s l11
L12           9 L11

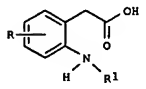
=> d ibib abs fhitstr hitrn 1-9
```

L12 ANSWER 1 OF 9 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 141:38434 CA
TITLE: Preparation of substituted amino phenylacetic acids and derivatives and their use as cyclooxygenase-2 (COX-2) inhibitors
INVENTOR(S): Fujimoto, Roger Aki; McQuire, Leslie Wighton; Monovich, Lauren G.; Mugrage, Benjamin Biro; Parker, David Thomas; Van Duzer, John Henry; Wattanasin, Sompong
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004048314	A1	20040610	WO 2003-EP13246	20031125
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SY, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2507458	AA	20040610	CA 2003-2507458	20031125
US 2004132769	A1	20040708	US 2003-724457	20031125
EP 1567477	A1	20050831	EP 2003-767652	20031125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

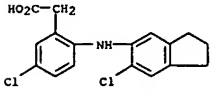
PRIORITY APPLN. INFO.: US 2002-429222P P 20021126
WO 2003-EP13246 W 20031125

OTHER SOURCE(S): MARPAT 141:38434
GI



AB The title compds. I (R = H, alkyl, cycloalkyl, halo, alkoxy, F3CO, Me3C, cyano, R1 = biaryl, β-naphthyl derivative, bicyclic heterocyclic aryl, cycloalkyl monocyclic carbocyclic aryl, cycloalkane fused-monocyclic carbocyclic aryl) were prepared Thus, N,N-dimethyl-2-(2',3',5',6'-tetrafluoro-4'-phenylanilino)phenylacetamide was hydrolyzed to give I (R =

L12 ANSWER 1 OF 9 CA COPYRIGHT 2005 ACS on STN (Continued)
H, R1 = 4-PhC6F4).
IT 702641-13-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (aminophenyl)acetic acid derivs. and their cyclooxygenase-2
inhibitory activity for treating rheumatoid arthritis, osteoarthritis, pain, dysmenorrhea, neoplasms, and inflammation)
RN 702641-13-2 CA
CN Benzeneacetic acid, 5-chloro-2-[(6-chloro-2,3-dihydro-1H-inden-5-yl)amino]- (9CI) (CA INDEX NAME)



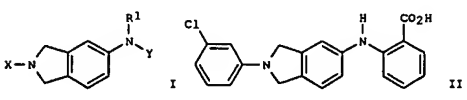
IT 702641-13-2P 702641-15-4P 702641-16-5P
702641-17-6P 702641-18-7P 702641-20-1P
702641-22-3P 702641-25-6P 702641-26-7P
702641-46-1P 702641-47-2P 702641-48-3P
702641-49-4P 702641-57-4P 702642-75-9P
702642-76-0P 702642-78-2P 702642-80-6P
702642-82-8P 702642-84-0P 702642-86-2P
702642-88-4P 702642-90-8P 702642-93-1P
702642-95-3P 702643-05-8P 702643-07-0P
702643-09-2P 702643-38-7P 702643-40-1P
702643-43-4P 702643-45-6P 702643-46-7P
702643-47-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (aminophenyl)acetic acid derivs. and their cyclooxygenase-2
inhibitory activity for treating rheumatoid arthritis, osteoarthritis, pain, dysmenorrhea, neoplasms, and inflammation)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 9 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 134:56565 CA
TITLE: Method of inhibiting amyloid protein aggregation, treating Alzheimer's disease, and imaging amyloid deposits using isoindoline derivatives
INVENTOR(S): Augelli-Szafran, Corinne Elizabeth; Lai, Yingjie; Sakkab, Annette Theresa; Walker, Lary Craswell
PATENT ASSIGNEE(S): Warner-Lambert Co., USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000076969	A1	20001221	WO 2000-US15073	20000531
W: AE, AG, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2373394	AA	20001221	CA 2000-2373394	20000531
AU 2000053120	A5	20010102	AU 2000-53120	20000531
AU 777747	B2	20041028		
BR 2000011446	A	20020319	BR 2000-11446	20000531
EP 1192131	A1	20020403	EP 2000-938023	20000531
EP 1192131	B1	20040804		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200200257	T2	20020621	TR 2002-200200257	20000531
JP 2003502313	T2	20030121	JP 2001-503829	20000531
EE 200100666	A	20030217	EE 2001-666	20000531
NZ 515619	A	20030530	NZ 2000-515619	20000531
AT 272623	E	20040815	AT 2000-938023	20000531
PT 1192131	T	20041130	PT 2000-938023	20000531
ES 2223531	T3	20050301	ES 2000-938023	20000531
ZA 2001009164	A	20030206	ZA 2001-9164	20011106
NO 2001005992	A	20020206	NO 2001-5992	20011207
BG 106291	A	20020531	BG 2002-106291	20020109
HK 1046283	A1	20050107	HK 2002-107877	20021030

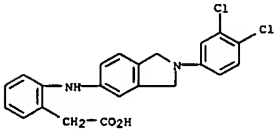
PRIORITY APPLN. INFO.: US 1999-138543P P 19990610
WO 2000-US15073 W 20000531

OTHER SOURCE(S): MARPAT 134:56565
GI



L12 ANSWER 2 OF 9 CA COPYRIGHT 2005 ACS on STN (Continued)

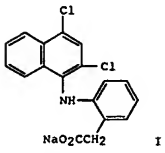
AB The invention provides a method of treating Alzheimer's disease using compds. I and their pharmaceutically acceptable salts [wherein: X = (un)substituted Ph; Y = (un)substituted Ph or (un)substituted pyridyl; substituents = (0-4 per ring) alkoxy, halo, alkyl, Ph, (un)substituted carbamoyl, CO2H, CO2R1, NO2, CF3, cyano, NR1R2, tetrazole, etc.; R1, R2 = H, C1-6 alkyl]. Also provided is a method of inhibiting the aggregation of amyloid proteins using I, and a method of imaging amyloid deposits using I. Claims further include compds. I, and pharmaceutical compns. containing I. Examples include 26 synthetic examples and 4 bioassays. For instance, title compound II was prepared by a sequence of: (1) imidation of 3-chloroaniline with 5-nitroisobenzofuran-1,3-dione (81%); (2) reduction of nitro to amino (99%); (3) reduction of the dione functions with AlCl3-LiAlH4 (58%), and (4) reaction with LiN(SiMe3)2 and 2-fluorobenzoic acid in THF (23%). In an assay for inhibition of self-seeded amyloid fibril growth, II had an IC50 of 1.1 μM. A combinatorial methodol. for preparation of I is also described.
IT 313532-79-5P, [2-[[2-(3,4-Dichlorophenyl)-2,3-dihydro-1H-isoindol-5-yl]amino]phenyl]acetic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of isoindoline derivs. as inhibitors of amyloid protein aggregation for treatment of Alzheimer's disease and imaging of amyloid deposits)
RN 313532-79-5 CA
CN Benzeneacetic acid, 2-[[2-(3,4-dichlorophenyl)-2,3-dihydro-1H-isoindol-5-yl]amino]- (9CI) (CA INDEX NAME)



IT 313532-79-5P, [2-[[2-(3,4-Dichlorophenyl)-2,3-dihydro-1H-isoindol-5-yl]amino]phenyl]acetic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of isoindoline derivs. as inhibitors of amyloid protein aggregation for treatment of Alzheimer's disease and imaging of amyloid deposits)

L12 ANSWER 2 OF 9 CA COPYRIGHT 2005 ACS on STN (Continued)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

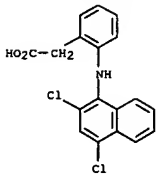
L12 ANSWER 3 OF 9 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 91:101950 CA
TITLE: Pharmacological studies of sodium [o-(2,4-dichloro-1-naphthylamino)phenyl]acetate (IG-243-Na)
AUTHOR(S): Fujinawa, Tomoaki; Morii, Isamu; Inagaki, Jinichiro; Muranaka, Mikio; Nakahashi, Takashi; Miyake, Hidekazu;
Kyo, Hitonobu; Fujimura, Hajime
CORPORATE SOURCE: Ikeda Mohando Co., Ltd., Toyama, Japan
SOURCE: Oyo Yakuri (1978), 16(2), 353-73
CODEN: OYYAA2; ISSN: 0369-8033
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
GI



I

AB IG 243 Na salt (I) [62809-33-0] (e.g., 32 mg/kg orally, in rats) inhibited the stages of the inflammatory responses: increase in capillary permeability, edema exudation, leukocyte migration, and granulation tissue formation. These activities of I were less potent than indomethacin and similar to Na diclofenac, but more potent than flufenamic acid or mefenamic acid. I also improved various inflammation parameters caused by adjuvant polyarthritis, and it had antipyretic and analgesic activities, but no anticonvulsant activity. I induced a transient increase in blood pressure, heart rate, and blood flow of cats, but had no effects in dogs. I decreased gastric secretion and intestinal motility, and its ulcerogenic activity in rat stomach was less than Na diclofenac, though the acute toxicity and protein-binding activity were comparatively stronger than the latter.
IT 62809-33-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(pharmacol. of)
RN 62809-33-0 CA
CN Benzeneacetic acid, 2-[(2,4-dichloro-1-naphthalenyl)amino]-, monosodium salt (9CI) (CA INDEX NAME)

L12 ANSWER 3 OF 9 CA COPYRIGHT 2005 ACS on STN (Continued)



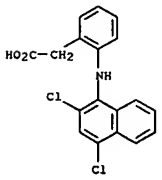
● Na

IT 62809-33-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(pharmacol. of)

L12 ANSWER 4 OF 9 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 88:98931 CA
TITLE: Studies of sulfhemoglobin formation by various drugs. 3
AUTHOR(S): Nomura, Akira
CORPORATE SOURCE: Dep. Pharmacol., Gifu Univ. Sch. Med., Gifu, Japan
SOURCE: Nippon Yakurigaku Zasshi (1977), 73(7), 793-802
CODEN: NYKZAU; ISSN: 0015-5691
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
GI

I

AB Diphenylamine-HCl [537-67-7], 1-naphthylamine-HCl (I-HCl) [552-46-5], phenyl-1-naphthylamine [90-30-2], N-(1-naphthyl)anthranilic acid [13278-41-6], and N-(1'-naphthyl)-2-aminophenylacetic acid [62809-19-2] injected i.p. into mice induced methemoglobinemia. I also induced sulfhemoglobinemia. Chemical structures in relation to abnormal blood pigment formation were discussed.
IT 62809-18-1
RL: BIOL (Biological study)
(metHb and sulfHb formation response to)
RN 62809-18-1 CA
CN Benzeneacetic acid, 2-[(2,4-dichloro-1-naphthalenyl)amino]- (9CI) (CA INDEX NAME)



IT 62809-18-1 62809-19-2 62809-26-1
RL: BIOL (Biological study)
(metHb and sulfHb formation response to)

L12 ANSWER 5 OF 9 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 88:22459 CA
TITLE: (Naphthylaminophenyl)acetic acids and their salts
INVENTOR(S): Nohara, Fujio; Fujinawa, Tomoaki; Ogawa, Kiyomi; Fujimura, Hajime
PATENT ASSIGNEE(S): Ikeda Mohando Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 30 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 52083822	A2	19770713	JP 1976-544	19760101
PRIORITY APPLN. INFO.:			JP 1976-544 A	19760101

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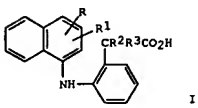


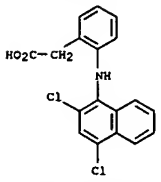
I

AB (Naphthylaminophenyl)acetic acids (I; R, R1 = H, alkyl, halo; R2 = H, alkyl; R3 = H, alkyl, substituted benzyl) and their alkali, alkaline earth, Al, and amine salts, effective analgesics, antiinflammatants, and antipyretics, were prepared Thus, 3.28 g 1-(2,4-dichloro-1-naphthyl)-2-indolinone was refluxed with 1 N NaOH in EtOH under N to give 62.5% I (R, R1 = 2,4-Cl2; R2 = R3 = H), which showed 46.30% inhibition against carrageenan edema at 30 mg/kg in rats. Similarly prepared were 15 addnl. I and salts.

IT **62809-18-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 62809-18-1 CA
CN Benzeneacetic acid, 2-[(2,4-dichloro-1-naphthalenyl)amino]- (9CI) (CA INDEX NAME)

L12 ANSWER 5 OF 9 CA COPYRIGHT 2005 ACS on STN (Continued)



IT **62809-18-1P 62809-19-2P 62809-20-5P 62809-24-9P 62809-25-0P 62809-26-1P 62809-27-2P 62809-28-3P 62809-31-8P 64959-76-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

L12 ANSWER 6 OF 9 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 87:151890 CA
TITLE: [o-(1-Naphthylamino)phenyl]acetic acids
INVENTOR(S): Nohara, Fujio; Fujinawa, Tomoaki; Ogawa, Kiyomi; Fujimura, Hajime
PATENT ASSIGNEE(S): Ikeda Mohando Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 52068160	A2	19770606	JP 1975-144244	19751203
PRIORITY APPLN. INFO.:			JP 1975-144244 A	19751203

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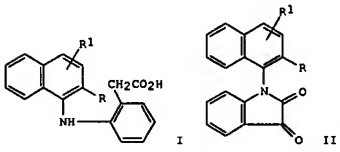


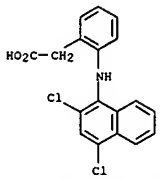
I II

AB Six title acids (I, R, R1 = Cl, 4-Cl; Me, 4-Cl; Cl, H; Cl, 4-Br; Me, 3-Me; Me, H; resp.) were prepared by reaction of indole-2,3-diones II with H2NNH2 or H2NCONHNH2 followed by heating in the presence of alkali to effect Wolff-Kishner reduction and hydrolysis. I had antipyretic, analgesic, and antiinflammatory activities (no data). Thus, a mixture of 20 g II (R = Cl, R1 = 4-Cl) and 7.6 g H2NNH2.H2O in diethylene glycol mono-Me ether was stirred 30 min at room temperature, 6.5 g powdered KOH added, the whole stirred 1 h at 150°, and acidified with N HCl to give 81.5% I (R = Cl, R1 = 4-Cl).

IT **62809-18-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 62809-18-1 CA
CN Benzeneacetic acid, 2-[(2,4-dichloro-1-naphthalenyl)amino]- (9CI) (CA INDEX NAME)

L12 ANSWER 6 OF 9 CA COPYRIGHT 2005 ACS on STN (Continued)



IT **62809-18-1P 62809-20-5P 62809-24-9P 62809-26-1P 62809-27-2P 62809-28-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

L12 ANSWER 7 OF 9 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 87:117726 CA
TITLE: [o-(1-Naphthylamino)phenyl]acetic acids
INVENTOR(S): Nohara, Fujio; Fujinawa, Tomoaki; Ogawa, Kiyomi; Fujimura, Hajime
PATENT ASSIGNEE(S): Ikeda Mohando Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 12 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 52068161	A2	19770606	JP 1975-144245	19751203
PRIORITY APPLN. INFO.:			JP 1975-144245 A	19751203

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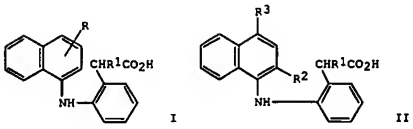
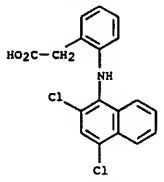


I II

AB Six title acids I (R, R1 = H, H; 2-Cl, H; 2-Cl, Me; H, Me; H, Me; 4-Me, H; 2-Me, H) were prepared by selective dehalogenation of II (R2 = Cl, Me; R3 = H, Me, Cl, Br) under reductive conditions. I had antipyretic, analgesic, and antiinflammatory activities (no data). Thus, 448 mL H was fed to a mixture of II (R1 = H, R2 = R3 = Cl) 3.46, NaOAc 1.7, and 10 % Pd/C 0.5 g in MeOH to give 53.2 % I (R = R1 = H).
IT **62809-18-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(dehalogenation of, reductive)
RN 62809-18-1 CA
CN Benzeneacetic acid, 2-[(2,4-dichloro-1-naphthalenyl)amino]- (9CI) (CA INDEX NAME)

L12 ANSWER 7 OF 9 CA COPYRIGHT 2005 ACS on STN (Continued)



IT **62809-18-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(dehalogenation of, reductive)
IT **62809-19-2P 62809-20-5P 62809-28-3P 62809-31-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

L12 ANSWER 8 OF 9 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 87:117725 CA
TITLE: [o-(2,4-Dichloro-1-naphthylamino)phenyl]acetic acid
INVENTOR(S): Nohara, Fujio; Fujinawa, Tomoaki; Ogawa, Kiyomi; Fujimura, Hajime
PATENT ASSIGNEE(S): Ikeda Mohando Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 52068159	A2	19770606	JP 1975-144243	19751203
PRIORITY APPLN. INFO.:			JP 1975-144243 A	19751203

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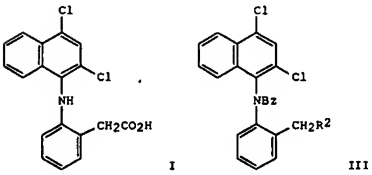
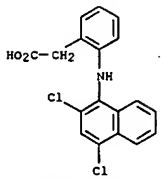


I III

AB Title acid (I) was prepared by Chapman rearrangement of (RO)PhC:NR1 II [R, R1 = 2,4-dichloro-1-naphthyl (Q), 2-R2CH2C6H4 (R2 = MeO2C, EtO2C, cyano)] followed by alkaline hydrolysis of the resulting III. I had antipyretic, analgesic, and antiinflammatory activities (no data). Thus, refluxing 17.5 g II (R = Q, R1 = 2-EtO2CCH2C6H4) in Ph2O 2 h under N gave 45.7 % III (R2 = EtO2C) (IV). Stirring 1 g IV with 7 g NaOH in aqueous dioxane 15 h under N gave, after treatment with N HCl, 69 % I.
IT **62809-18-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 62809-18-1 CA
CN Benzeneacetic acid, 2-[(2,4-dichloro-1-naphthalenyl)amino]- (9CI) (CA INDEX NAME)

L12 ANSWER 8 OF 9 CA COPYRIGHT 2005 ACS on STN (Continued)

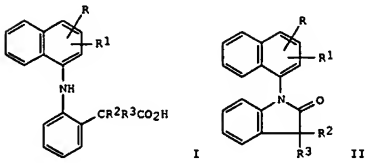


IT **62809-18-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

L12 ANSWER 9 OF 9 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 87:5725 CA
TITLE: Naphthylaminophenylacetic acid derivatives
INVENTOR(S): Nohara, Fujio; Fujinawa, Tomoaki; Ogawa, Kiyomi; Fujimura, Hajime
PATENT ASSIGNEE(S): Ikeda Mohando Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 14 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 51149252	A2	19761222	JP 1975-72474	19750614
PRIORITY APPLN. INFO.:			JP 1975-72474 A	19750614

GI



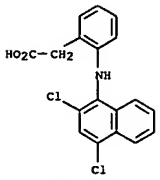
AB [2-(1-Naphthylamino)phenyl]acetic acid derivs. I (R, R1 = H, alkyl, F, Cl, Br; R2 = H, alkyl; R3 = H, alkyl, PhCH2, substituted benzyl) and their salts were prepared by alkaline hydrolysis of II. I had antipyretic, analgesic, and antiinflammatory activities. Thus, reflux of 3.28 g II (R = 2-Cl, R1 = 4-Cl, R2 = R3 = H) and N NaOH in EtOH 14 h gave 62.5% I (R = 2-Cl, R1 = 4-Cl, R2 = R3 = H), which showed 46.30% inhibition of carrageenan edema in rats.

IT **62809-18-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of)

RN 62809-18-1 CA

CN Benzeneacetic acid, 2-[(2,4-dichloro-1-naphthalenyl)amino]- (9CI) (CA INDEX NAME)

L12 ANSWER 9 OF 9 CA COPYRIGHT 2005 ACS on STN (Continued)



IT **62809-18-1P 62809-19-2P 62809-20-5P**
62809-24-9P 62809-25-0P 62809-26-1P
62809-27-2P 62809-28-3P 62809-31-8P
62809-33-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of)

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L3          141 S L1 FULL

     FILE 'CA' ENTERED AT 10:30:25 ON 07 SEP 2005
L4            1 S L3

     FILE 'MARPAT' ENTERED AT 10:30:40 ON 07 SEP 2005
L5           60 S L1 FULL
L6           59 S L5/COM

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L7              STRUCTURE UPLOADED
L8              STRUCTURE UPLOADED
L9          626 S L7 FULL
L10         580 S L8 FULL
L11          46 S L9 NOT L10

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L12           9 S L11

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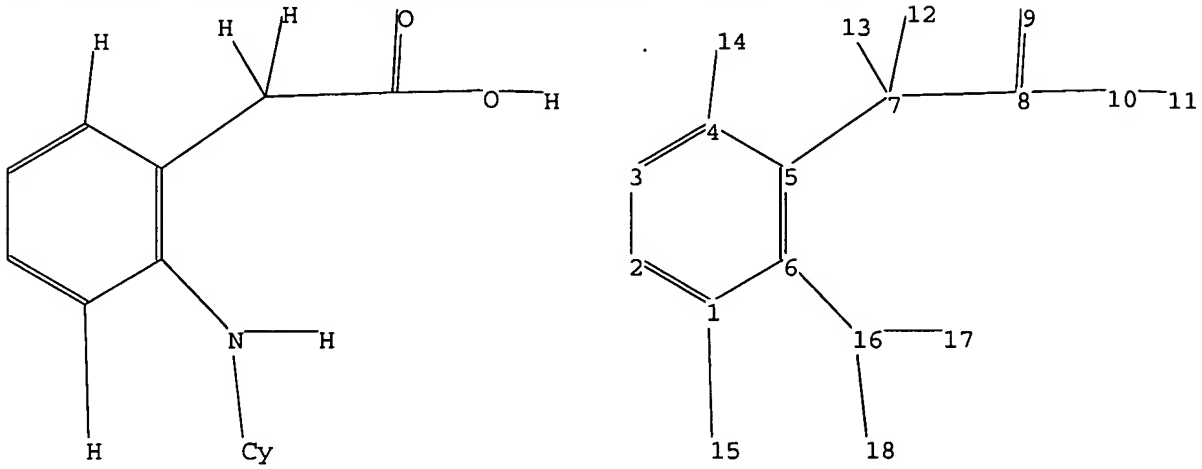


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ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6
exact/norm bonds :
6-16  16-18
exact bonds :
1-15  4-14  5-7  7-8  7-12  7-13  10-11  16-17
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6  8-9  8-10
isolated ring systems :
containing 1 :


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:CLASS  8:CLASS  9:CLASS  10:CLASS
 11:CLASS  12:CLASS  13:CLASS  14:CLASS  15:CLASS  16:CLASS  17:CLASS  18:Atom



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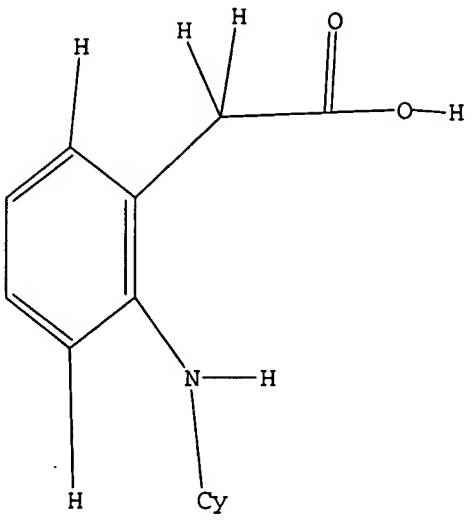

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L2 43 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
IN Benzeneacetic acid, 5-chloro-2-[(2,3,4',5-tetrafluoro[1,1'-biphenyl]-4-yl)amino]- (9CI)
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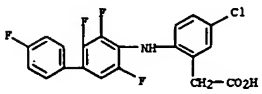

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HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

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=> s l6 and l4
L7          76 L6 AND L4

=> s l7 and inhibitor
        471828 INHIBITOR
L8          56 L7 AND INHIBITOR

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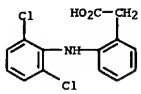
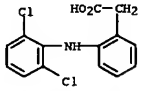
L8 ANSWER 1 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 140:169654 CA
TITLE: Oral pharmaceutical formulations containing alkaline agents and binders
INVENTOR(S): Kositprapa, Unchalee
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 9 pp., Cont.-in-part of U.S. Ser. No. 597,206.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 2004028735	A1	20040212	US 2003-634321	20030804	
US 6096340	A	20000801	US 1997-970489	19971114	<--
US 6174548	B1	20010116	US 1998-143167	19980828	<--
US 6077541	A	20000620	US 1999-335575	19990618	<--
US 6602522	B1	20030805	US 2000-597206	20000620	
US 2003113376	A1	20030619	US 2002-279622	20021023	
US 6780435	B2	20040824			
PRIORITY APPLN. INFO.:			US 1997-970489	A3 19971114	
			US 1998-143167	A2 19980828	
			US 1999-335575	A2 19990618	
			US 2000-597206	A2 20000620	
			US 2000-607293	B1 20000630	

AB An oral pharmaceutical formulation, e.g., a tablet core, contains an uncoated granule of a drug, an optional surfactant, an alkaline agent and a combination of a water-soluble binder and a water-insol. binder. The controlled release of drugs is achieved by way of the water soluble and water insol. binders. The formulation for making granules contained: Eudragit NE30D 33.0, Plasdone K30 98.0, sodium lauryl sulfate 6.0, Avicel PH102 1439.0, felodipine 244.0, and water 1600.0 g. The granules were formed into tablets by compressing felodipine granules 160.7, glyceryl monostearate 13.5, Crospovidone 79.6, and Avicel PH101 16.2 g.
IT 15307-86-5, Diclofenac
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral pharmaceutical formulations containing alkaline agents and binders)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



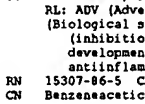
L8 ANSWER 2 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 138:378847 CA
TITLE: Nimesulide and rofecoxib tolerance in patients with allergy to nonsteroidal anti-inflammatory drugs
AUTHOR(S): Ortega, N.; Castillo, R.; Blanco, C.; Carrillo, T.
CORPORATE SOURCE: Allergy Unit, Hospital de Gran Canaria Dr Negrin, Canary Islands, 35012, Spain
SOURCE: Recent Research Developments in Allergy, Asthma & Immunology (2003), 1, 121-128
CODEN: RRDAFM
PUBLISHER: Transworld Research Network
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Some patients with aspirin-sensitive respiratory or cutaneous disease experience cross-reactivity with ASA (acetylsalicylic acid) and other nonsteroidal antiinflammatory drugs (NSAIDs) with different chemical structure which inhibit cyclooxygenase enzymes (COX). Recently, nimesulide and rofecoxib have been introduced. These drugs are a weak inhibitor of COX-1, and selective inhibitor of the COX-2, resp. We evaluate the clin. characteristics of controlled oral challenges carried out in patients with sensitivity to NSAIDs. To clarify the prevalence of nimesulide and rofecoxib cross-reactivity, we performed a prospective study on these subjects with sensitivity to NSAIDs by administering sequential challenge doses of nimesulide and rofecoxib. During five months, consecutive subjects come to the Allergy Service with histories of NSAIDs reactions and were recruited for the study. Patients were included in a previously established double-blind placebo-controlled drug challenge (DBPCDC)protocol. If the symptoms developed during the day the placebo was administered, or the DBPCDCs were neg. with different drugs administered, the patient was dropped from the study. All subjects pos. to DBPCDC were assigned to perform a DBPCDC with nimesulide and rofecoxib. Forty six patients had a pos. challenge with some NSAIDs. Thirty one patients were women, with a mean age of 23 yr (range 12 to 59 yr). Isolated angioedema was the most common previous reaction. Thirty eight patients were atopic. In order of frequency, the drugs most commonly involved in the pos. challenges were ASA and diclofenac. Three (6.5 %) patients reacted with nimesulide. No differences were found in age, sex, or atopy. Patients who had cutaneous or respiratory reaction with nimesulide, also reacted similarly to NSAIDs. We found that the nimesulide-induced reactions were milder than those induced by other NSAIDs. When rofecoxib was administered, we did not find any adverse reactions. In the present study, the tolerance to nimesulide and rofecoxib during DBPCDC can indicate a safe, currently available alternative for patients with NSAIDs-sensitivity, respiratory or cutaneous disease. We recommend doing a test dose for this patient rather then simply suggesting the use of the nimesulide at home. However, this study does not exclude that rofecoxib can produce other types of adverse reactions. The mechanism involved patient with nonsteroidal antiinflammatory sensitivity are very linked to the effects of inhibition of COX-1.
IT 15307-86-5, Diclofenac
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nimesulide and rofecoxib treatment in patients with allergy to nonsteroidal anti-inflammatory drugs)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

L8 ANSWER 3 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 137:72807 CA
TITLE: Inhibition of both COX-1 and COX-2 is required for development of gastric damage in response to nonsteroidal antiinflammatory drugs
AUTHOR(S): Tanaka, A.; Araki, H.; Komoike, Y.; Hase, S.; Takeuchi, K.
CORPORATE SOURCE: Department of Pharmacology and Experimental Therapeutics, Kyoto Pharmaceutical University, Misasagi, Yamashina, Kyoto, 607-8414, Japan
SOURCE: Journal of Physiology (Paris) (2001), 95(1-6), 21-27
CODEN: JHYSEM; ISSN: 0928-4257
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We examined the gastric ulcerogenic property of selective COX-1 and/or COX-2 inhibitors in rats, and investigated whether COX-1 inhibition is by itself sufficient for induction of gastric damage. Animals fasted for 18 h were given various COX inhibitors p.o., either alone or in combination, and they were killed 8 h later. The non-selective COX inhibitors such as indomethacin, naproxen and diclofenac inhibited prostaglandin (PG) production, increased gastric motility, and provoked severe gastric lesions. In contrast, the selective COX-2 inhibitor rofecoxib did not induce any damage in the stomach, with no effect on the mucosal PGE2 contents and gastric motility. Likewise, the selective COX-1 inhibitor SC-560 also did not cause gastric damage, despite causing a significant decrease in PGE2 contents. The combined administration of SC-560 and rofecoxib, however, provoked gross damage in the gastric mucosa, in a dose-dependent manner. SC-560 also caused a marked gastric hypermotility, whereas rofecoxib had no effect on basal gastric motor activity. On the other hand, the COX-2 mRNA was expressed in the stomach after administration of SC-560, while the normal gastric mucosa expressed only COX-1 mRNA but not COX-2 mRNA. These results suggest that the gastric ulcerogenic property of conventional NSAIDs is not accounted for solely by COX-1 inhibition and requires the inhibition of both COX-1 and COX-2. The inhibition of COX-1 up-regulates the COX-2 expression, and this may counteract the deleterious influences, such as gastric hypermotility and the subsequent events, due to a PG deficiency caused by COX-1 inhibition.
IT 15307-86-5, Diclofenac
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of both COX-1 and COX-2 is required for development of gastric damage in response to nonsteroidal antiinflammatory drugs (NSAIDS))
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

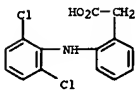


REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)

L8 ANSWER 4 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 137:57174 CA
TITLE: In vitro effects of cyclooxygenase inhibitors in whole blood of horses, dogs, and cats
AUTHOR(S): Brideau, Christine; Van Staden, Carlo; Chan, Chi Chung
CORPORATE SOURCE: Departments of Biochemistry & Molecular Biology, Merck Frosst Centre for Therapeutic Research, Kirkland, QC, H9R 4P8, Can.
SOURCE: American Journal of Veterinary Research (2001), 62(11), 1755-1760
CODEN: AJVRAH; ISSN: 0002-9645
PUBLISHER: American Veterinary Medical Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The objective was to determine potency and selectivity of nonsteroidal anti-inflammatory drugs (NSAID) and cyclooxygenase (COX) specific inhibitors in whole blood from horses, dogs, and cats. Activities of COX-1 and COX-2 were determined by measuring coagulation-induced thromboxane B2 and lipopolysaccharide-induced prostaglandin E2 concns., resp., in whole blood with and without the addition of various concns. of phenylbutazone, flunixin meglumine, ketoprofen, diclofenac, indomethacin, meloxicam, carprofen, 5-bromo-2[4-fluorophenyl]-3-[4-methylsulfonylphenyl]-thiophene (DuP 697), 5,5-dimethyl-3-(3-fluorophenyl)-4-(4-methylsulfonyl) phenyl-2(5H)-furanone (DFU), 3-(3,4-difluorophenyl)-4-(4-(methylsulfonyl)phenyl)-2-(5H)-furanone (MF-tricyclic), and celecoxib. Potency of each test compound was determined by calculating the concentration that resulted in inhibition of 50% of COX activity (IC50). Selectivity was determined by calculating the ratio of IC50 for COX-1 to IC50 for COX-2 (COX-1/COX-2 ratio). The novel compound DFU was the most selective COX-2 inhibitor in equine, canine, and feline blood; COX-1/COX-2 ratios were 77.5, 74, and 69, resp. Carprofen was the weakest inhibitor of COX-2, compared with the other COX-2 selective inhibitors, and did not inhibit COX-2 activity in equine blood. In contrast, NSAID such as phenylbutazone and flunixin meglumine were more potent inhibitors of COX-1 than COX-2 in canine and equine blood. Conclusions and Clin. Relevance-The novel COX-2 inhibitor DFU was more potent and selective in canine, equine, and feline blood, compared with phenylbutazone, flunixin meglumine, and carprofen. Compds. that specifically inhibit COX-2 may result in a lower incidence of adverse effects, compared with NSAID, when administered at therapeutic dosages to horses, dogs, and cats.
IT 15307-86-5, Diclofenac
RL: PAC (Pharmacological activity); BIOL (Biological study)
(in vitro effects of cyclooxygenase inhibitors in whole blood of horses, dogs, and cats)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

L8 ANSWER 4 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 136:221745 CA
TITLE: Irrigation solution and method for inhibition of pain and inflammation
INVENTOR(S): Demopulos, Gregory A.; Pierce-Palmer, Pamela; Herz, Jeffrey M.
PATENT ASSIGNEE(S): Omeros Medical Systems, USA
SOURCE: U.S. Pat. Appl. Publ., 58 pp., Cont.-in-part of Appl. No. PCT/US99/24625.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002028798	A1	20020307	US 2001-839633	20010420
WO 9619233	A2	19960627	WO 1995-US16028	19951212 <--
WO 9619233	A3	19960919		
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US 5820583	A	19981013	US 1996-670699	19960626 <--
US 6261279	B1	20010717	US 1998-72913	19980504 <--
WO 2000023061	A2	20000427	WO 1999-US24557	19991020 <--
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WO 2000023066	A2	20000427	WO 1999-US24672	19991020 <--
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L8 ANSWER 5 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)

AU 2000011277	A5	20000508	AU 2000-11277		19991020 <--
EP 1261334	A1	20021204	EP 1999-955097		19991020
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US 2003087962	A1	20030508	US 2002-138193		20020501
US 2003096807	A1	20030522	US 2002-138192		20020501
US 2003235589	A1	20031225	US 2003-356649		20030131
PRIORITY APPLN. INFO.:			US 1994-353775	B2	19941212
			WO 1995-US16028	A2	19951212
			US 1996-670699	A2	19960626
			US 1998-72913	A2	19980504
			US 1998-105026P	P	19981020
			US 1998-105029P	P	19981020
			US 1998-105044P	P	19981020
			US 1998-105166P	P	19981021
			US 1998-107256P	P	19981105
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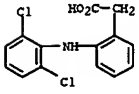
			WO 1999-US24625	A2	19991020
			WO 1999-US24672	A2	19991020
			WO 1999-US26330	A2	19991105
			US 1999-144904P	P	19990721
			WO 2000-US19864	W	20000721
			US 2001-839633	A2	20010420
			US 2002-31546	A2	20020118
			US 2002-353552P	P	20020201

AB A method and solution for perioperatively inhibiting a variety of pain and inflammation processes at wounds from general surgical procedures including oral/dental procedures. The solution preferably includes at least one pharmacol. agent selected from the group consisting of a mitogen-activated protein kinase (MAPK) inhibitor, an α2-receptor agonist, a neuronal nicotinic acetylcholine receptor agonist, a cyclooxygenase-2 (COX-2) inhibitor , a soluble receptor and mixts. thereof, and optionally addnl. multiple pain and inflammation inhibitory agents at dilute concentration in a physiol. carrier, such as saline or lactated Ringer's solution The solution is applied by continuous irrigation of a wound during a surgical procedure for preemptive inhibition of pain and while avoiding undesirable side effects associated with oral, i.m., s.c. or i.v. application of larger doses of the agents.

IT 15307-86-5, Diclofenac
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(irrigation solution for inhibition of pain and inflammation at wounds during surgical procedures)

RN 15307-86-5 CA

CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



L8 ANSWER 6 OF 56 CA COPYRIGHT 2005 ACS on STN

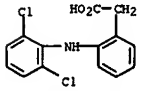
ACCESSION NUMBER:	136:177656 CA
TITLE:	Relationship between endogenous colony stimulating factors and apoptosis in human colon cancer cells: role of cyclo-oxygenase inhibitors
AUTHOR(S):	Calatayud, Sara; Warner, Timothy D.; Breese, Emma J.; Mitchell, Jane A.
CORPORATE SOURCE:	Unit of Critical Care, The Royal Brompton and Harefield N.H.S. Trust, Imperial College School of Medicine, London, SW 6NP, UK
SOURCE:	British Journal of Pharmacology (2001), 134(6), 1237-1244 CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER:	Nature Publishing Group
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Nonsteroidal anti-inflammatory drug (NSAID) usage is associated with gastrointestinal inflammatory damage and aggravation of gut inflammatory conditions. NSAIDs also exert a preventive effect against colon cancer that seems to be due to increased colon cell apoptosis. NSAIDs have been shown to modulate the release of colony stimulating factors (CSFs) in some cells. In the present study we analyzed the effect of these drugs on secretion of CSFs and apoptosis in human colon epithelial cells (HT-29). HT-29 cells secreted bioactive levels of GM-CSF, G-CSF and M-CSF when stimulated with IL-1β and TNF-α, and diclofenac (10-7-10-4 M), indomethacin (10-7-10-4 M) and sodium salicylate (10-5-10-2 M) induced concentration-dependent increases in GM-CSF secretion. Reduced secretion of G-CSF and M-CSF and increased cell apoptosis were observed with the highest concns. of these non-selective NSAIDs. No changes in any CSF release or HT-29 cell apoptosis were detected in the presence of the COX-2 selective inhibitor DFP (10-7-10-4 M). Neither the exogenous addition of CSFs nor the blockade of secreted CSFs modified apoptosis in HT-29 cells stimulated with cytokines and/or NSAIDs. These results suggest that colon epithelial cells can contribute to local inflammatory responses by releasing CSFs and thus extend the life span of local leukocytes. Modulation of CSF levels by non-selective NSAIDs may be involved in the pro-inflammatory effects of these agents in the gut.

IT 15307-86-5, Diclofenac
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(relationship between endogenous colony stimulating factors and apoptosis in human colon cancer cells and role of cyclo-oxygenase inhibitors)

RN 15307-86-5 CA

CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 56 CA COPYRIGHT 2005 ACS on STN

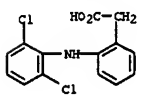
ACCESSION NUMBER:	136:144877 CA
TITLE:	Identification of Dual Cyclooxygenase-Eicosanoid Oxidoreductase Inhibitors: NSAIDs That Inhibit PG-LX Reductase/LTB4 Dehydrogenase
AUTHOR(S):	Clish, Clary B.; Sun, Yee-Ping; Serhan, Charles N.
CORPORATE SOURCE:	Center for Experimental Therapeutics and Reperfusion Injury, Department of Anesthesiology, Perioperative and Pain Medicine, Brigham & Women's Hospital and Harvard Medical School, Boston, MA, 02115, USA
SOURCE:	Biochemical and Biophysical Research Communications (2001), 288(4), 868-874 CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER:	Academic Press
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Eicosanoids play key roles in many physiol. and disease processes, and their regulation by nonsteroidal anti-inflammatory drugs (NSAIDs) is critical to many therapeutic approaches. These autacoids are rapidly inactivated by specific enzymes such as 15-hydroxyprostaglandin dehydrogenase (15-PGDH) and 15-oxoprostaglandin 13-reductase/leukotriene B4 12-hydroxydehydrogenase (PGR/LTB4DH) that act on main series of eicosanoids (i.e., leukotrienes, prostaglandins), and recently found to act in lipoxin inactivation. Here, a panel of NSAIDs was assessed to determine each compound's ability to inhibit eicosanoid-directed activities of either the recombinant 15-PGDH or the PG-LXR/LTB4DH. The recombinant 15-PGDH that acts on both prostaglandin E2 (PGE2) and lipoxin A4 (LXA4) was not significantly inhibited by the NSAIDs tested. In contrast, several of the widely used NSAIDs were potent inhibitors of the PG-LXR/LTB4DH that metabolizes 15-oxo-PGE2, and LTB4 as well as 15-oxo-LXA4. Diclofenac and indomethacin each inhibited PG-LXR/LTB4DH-catalyzed conversion of 15-oxo-PGE2 to 13,14-dihydro-15-oxo-PGE2 by 70 and 95%, resp. Also, a COX-2 inhibitor, niflumic acid, inhibited the PG-LXR/LTB4DH eicosanoid oxidoreductase (EOR) by 80% while other COX-2 inhibitors such as nimesulide and NS-398 did not inhibit this enzyme. These results indicate that certain clin. useful NSAIDs such as diclofenac and indomethacin, in addition to inhibiting cyclooxygenases (1 and 2), also interfere with eicosanoid degradation by blocking PG-LXR/LTB4DH (EOR) and are members of a new class of dual cyclooxygenase (COX)-EOR inhibitors. Moreover, they suggest that the impact of NSAIDs on PG-LXR/LTB4DH activities as targets in the local tissue regulation of eicosanoid-mediated processes should be taken into account. (c) 2001 Academic Press.

IT 15307-86-5, Diclofenac
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(identification of NSAIDS that are dual cyclooxygenase-eicosanoid oxidoreductase inhibitors)

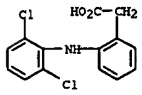
RN 15307-86-5 CA

CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



L8 ANSWER 7 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

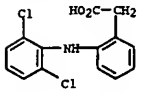
L8 ANSWER 8 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 136:129292 CA
TITLE: Anti-inflammatory effect of synthetic somatostatin analogues in the rat
AUTHOR(S): Helyes, Zsuzsanna; Pinter, Erika; Nemeth, Jozsef; Keri, Gyorgy; Than, Marta; Oroszi, Gabor; Horvath, Aniko; Szolcsanyi, Janos
CORPORATE SOURCE: Department of Pharmacology and Pharmacotherapy, Faculty of Medicine, University of Pecs, Pecs, H-7643, Hung.
SOURCE: British Journal of Pharmacology (2001), 134(7), 1571-1579
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Somatostatin (6.11 nmol kg-1 i.p.) inhibited neurogenic plasma extravasation evoked by 1% mustard oil and non-neurogenic edema induced by 5% dextran in the rat skin. Cyclic synthetic octapeptide (TT-248 and TT-250) and heptapeptide (TT-232) somatostatin analogs proved to be more effective in reducing neurogenic and non-neurogenic inflammatory reactions but octreotide had no influence on either neurogenic or non-neurogenic inflammation. TT-232 administered i.p. or i.v. (1.06-42.40 nmol kg-1) inhibited in a dose-dependent manner the plasma extravasation evoked by mustard oil in the rat's paw. Neither diclofenac (15.78-315.60 μmol kg-1) nor the selective COX-2 inhibitor meloxicam (2.95-569.38 μmol kg-1) attenuated the mustard oil-induced neurogenic plasma extravasation. TT-232, diclofenac and meloxicam dose-dependently diminished non-neurogenic dextran-edema of the paw the ED35 values were 1.73 nmol kg-1 for TT-232 and 34.37 μmol kg-1 for diclofenac. TT-232 inhibited in the dose range of 1.06-21.21 nmol kg-1 the bradykinin-induced plasma extravasation in the skin of the chronically denervated paw. Mustard oil-induced cutaneous plasma extravasation was dose-dependently diminished by s.c. TT-232 1, 2, 4, 6 or 16 h after the treatment. TT-232 (2 + 106, 2 + 212 and 2 + 530 nmol kg-1 per day s.c. for 18 days) caused dose-dependent inhibition of chronic Freund adjuvant-induced arthritis during the exptl. period. TT-232 (200 and 500 nM) inhibited the release of SP, CGRP and somatostatin from the rat isolated trachea induced by elec. field stimulation (40 V, 0.1 ms, 10 Hz, 120 s) or by capsaicin (10-7 M), but did not influence the basal, non-stimulated peptide release. It is concluded that somatostatin analogs without endocrine functions as TT-232 are promising compds. with a novel site of action for inhibition of non-neurogenic and neurogenic inflammatory processes.
IT 15307-86-5, Diclofenac
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(anti-inflammatory effect of synthetic somatostatin analogs in rat)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



L8 ANSWER 8 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 136:79446 CA
TITLE: A comparison of renal-related adverse drug reactions between rofecoxib and celecoxib, based on the World Health Organization/Uppsala Monitoring Centre safety database
AUTHOR(S): Zhao, Sean Z.; Reynolds, Matthew W.; Lefkowith, James; Whelton, Andrew; Arellano, Felix M.
CORPORATE SOURCE: Pharmacia Corporation, Peapack, NJ, USA
SOURCE: Clinical Therapeutics (2001), 23(9), 1478-1491
CODEN: CLTHDG; ISSN: 0149-2918
PUBLISHER: Excerpta Medica, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two isoforms of cyclooxygenase (COX) have been identified, both of them inhibited by traditional nonsteroidal anti-inflammatory drugs (NSAIDs). Inhibition of COX-2 has been associated with the therapeutic effects of NSAIDs, whereas inhibition of COX-1 is believed to be the cause of the adverse gastrointestinal effects associated with NSAID therapy. When administered at therapeutic doses, new COX-2-specific inhibitors inhibit only the COX-2 isoform. This study sought to compare renal safety signals between the COX-2-specific inhibitors rofecoxib and celecoxib, based on spontaneous reports of adverse drug reactions (ADRs) in the World Health Organization/Uppsala Monitoring Center (WHO/UMC) safety database through the end of the second quarter 2000. Disproportionality in the association between a particular drug and renal-related ADR was evaluated using a bayesian confidence propagation neural network method in which a statistical parameter, the information component (IC) value, was calculated for each drug-ADR combination. In this method, an IC value significantly greater than 0 implies that the association of a drug-ADR pair is stronger than background; the higher the IC value, the more the combination stands out from the background. The ratio of actual to expected nos. of ADRs was also used to assess disproportionality. As with traditional NSAIDs, both COX-2-specific inhibitors were associated with renal-related ADRs. However, the adverse renal impact of rofecoxib was significantly greater than that of celecoxib. IC values were significantly different for the following comparisons: water retention (1.97 rofecoxib vs 1.18 celecoxib; $P < 0.01$); abnormal renal function (2.38 vs 0.70; $P < 0.01$); renal failure (2.22 vs 1.09; $P < 0.01$); cardiac failure (2.39 vs 0.48; $P < 0.01$); and hypertension (2.15 vs 1.33; $P < 0.01$). In an addnl. anal., celecoxib was shown to have a similar renal safety profile to that of diclofenac and ibuprofen. Based on spontaneous ADR reports in the WHO/UMC safety database at the end of the second quarter 2000, this anal. indicates that rofecoxib has significantly greater renal toxicity than celecoxib or traditional NSAIDs. This neg. renal impact may have the potential to increase the risk for serious cardiac and/or cerebrovascular events.
IT 15307-86-5, Diclofenac
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparison of rofecoxib and celecoxib renal-related adverse drug reactions in humans)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

L8 ANSWER 9 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)

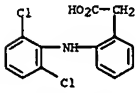


REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 136:15235 CA
TITLE: Protected forms of a conjugate combination of nonsteroidal antiinflammatory drugs (NSAIDs) and cyclooxygenase 2 (COX-2) inhibitors, and their therapeutic use
INVENTOR(S): Lai, Ching-San; Wang, Tingmin
PATENT ASSIGNEE(S): Medinox, Inc., USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001093680	A1	20011213	WO 2001-US17480	20010530 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6306842	B1	20011023	US 2000-586344	20000602 <--
PRIORITY APPLN. INFO.:			US 2000-586344	A1 20000602
			US 2000-588993	A1 20000606

AB The invention provides conjugates of a combination of pharmacol. active agents (e.g., NSAIDs and selective COX-2 inhibitors). The conjugates provide a new class of pharmacol. active agents (e.g., anti-inflammatory agents) which provide the therapeutic benefits of both NSAIDs and selective COX-2 inhibitors, while causing a much lower incidence of side-effects then are typically observed with such agents due to the protective effects imparted by modifying the pharmacol. active agents.
IT 15307-86-5D, Diclofenac, conjugates with COX-2 inhibitors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NSAID-COX-2 inhibitor conjugates, and therapeutic use)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



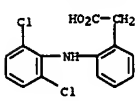
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)

L8 ANSWER 11 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:298780 CA
TITLE: Conjugates of antiinflammatory or other pharmacologically active agents, their preparation, and their therapeutic use
INVENTOR(S): Lai, Ching-San; Wang, Tingmin
PATENT ASSIGNEE(S): Medinox, Inc., USA
SOURCE: U.S., 10 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

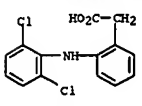
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6306842	B1	20011023	US 2000-586344	20000602 <--
WO 2001093680	A1	20011213	WO 2001-US17480	20010530 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2000-586344	A1 20000602
			US 2000-588993	A1 20000606

AB Conjugates of a combination of pharmacol. active agents (e.g., NSAIDs and selective COX-2 inhibitors) are provided. These conjugates provide a new class of pharmacol. active agents (e.g., anti-inflammatory agents) which provide the therapeutic benefits of both NSAIDs and selective COX-2 inhibitors, while causing a much lower incidence of side-effects then are typically observed with such agents due to the protective effects imparted by modifying the pharmacol. active agents.
IT 15307-86-5D, Diclofenac, COX-2 inhibitor conjugates
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates of antiinflammatory or other pharmacol. active agents, preparation, and therapeutic use)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



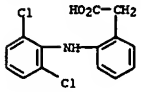
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:282613 CA
TITLE: In-vitro test system for the evaluation of cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) inhibitors based on a single HPLC run with UV detection using bovine aortic coronary endothelial cells (BAECs)
AUTHOR(S): Dannhardt, G.; Ulbrich, H.
CORPORATE SOURCE: Institute of Pharmacy, University of Mainz, Mainz, D-55099, Germany
SOURCE: Inflammation Research (2001), 50(5), 262-269
CODEN: INREFB; ISSN: 1023-3830
PUBLISHER: Birkhaeuser Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Objective and Design: The aim of this study was to develop a new, whole-cell test system which is easy to handle and requires a standard equipment for the parallel screening of COX-1 and COX-2 inhibitors. Materials: Bovine aortic endothelial cells (BAECs). Treatment and methods: Unstimulated bovine aortic coronary endothelial cells (BAECs) were used as a source of COX-1 and BAECs pretreated with ASA (100 μM) and activated with phorbol myristate acetate (PMA) were used as a source of COX-2. The time- and concentration-dependent induction of COX-2 expression in the BAECs was evaluated by a kinetic profile (HPLC anal.) and detected by Western-Blot anal. using polyclonal antibodies against COX-1 and COX-2. Results: In BAECs, diclofenac and meloxicam showed balanced inhibition of COX-1 (IC50: 0.01/0.4 μM) and COX-2 (IC50: 0.03/0.6 μM). Indomethacin inhibited COX-1 more potently than COX-2 (IC50: 0.008/0.04 μM). Aceclofenac inhibited COX-2 more potently than COX-1 (IC50: 3.0/7.3 μM). DFU and Cl-SC57666 [16] inhibited COX-2 (IC50: 0.04/0.001 μM) highly selectively but did not inhibit COX-1 (IC50: > 100 μM). Conclusions: In summary an assay has been developed, for the determination of IC50-values for inhibitors of COX-1/2 on cells of the same origin, in line with values in the literature. Moreover, new insights have been gained into the relation of COX-1/2 and lipoxygenase pathways in BAECs by detecting 15- and 12-HETE: Inhibition of COX-1 by the NSAIDs mostly resulted in an enhancement of 15-HETE and 12-HETE release. In contrast inhibition of COX-2 decreased 15-HETE release.
IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(In-vitro test system for evaluation of cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) inhibitors based on a single HPLC run with UV detection using bovine aortic coronary endothelial cells (BAECs))
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)

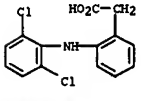


REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:220913 CA
TITLE: In vitro based index of topical anti-inflammatory activity to compare a series of NSAIDs
AUTHOR(S): Cordero, J. A.; Camacho, M.; Obach, R.; Domenech, J.; Vila, L.
CORPORATE SOURCE: Faculty of Pharmacy, Pharmacokinetics and Biopharmaceutics Unit, University of Barcelona, Barcelona, Spain
SOURCE: European Journal of Pharmaceutics and Biopharmaceutics (2001), 51(2), 135-142
CODEN: EJPBEL; ISSN: 0939-6411
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The aim of the present work was to generate an index to predict topical efficiency of a series of nonsteroidal anti-inflammatory drugs (NSAIDs): indomethacin, diclofenac, ketoprofen, piroxicam, tenoxicam and ketorolac. This index took into account both biopharmaceutic and pharmacodynamic aspects. The biopharmaceutic aspect, based on the maximal flux (Jm), was determined exptl. from transdermal studies carried out with human skin in previous work. The pharmacodynamic aspect, based on the ability to inhibit cyclooxygenase-2 (COX-2) in vitro, was determined by incubating human dermal fibroblasts in culture, pre-treated with phorbol-12-myristate-13-acetate (PMA) for 6 h, with 25 μM [14C]-arachidonic acid (AA) in the presence of several drug concns. The most potent inhibitor of COX-2 activity in induced fibroblasts was diclofenac while indomethacin, ketoprofen and ketorolac were approx. equipotent. Piroxicam and tenoxicam were inhibitors at higher concns. Based on the proposed index of the topical anti-inflammatory activity (ITAA) diclofenac, ketorolac, ketoprofen and indomethacin exhibited acceptable efficiency for external use. However, piroxicam and tenoxicam showed the lowest topical anti-inflammatory activity of the series assayed. In conclusion, indomethacin ketorolac, ketoprofen and diclofenac have shown good intrinsic feasibility for formulation into topical pharmaceutical forms. However, for dermatol. formulations of oxicams, use of penetration enhancers may be unavoidable.
IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(in vitro based index of topical anti-inflammatory activity to compare a series of NSAIDs in relation to transdermal flux and COX-2 inhibition)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:190345 CA
TITLE: Inhibition of COX in ocular tissues: an in vitro model to identify selective COX-2 inhibitors
AUTHOR(S): Garcia-Cabanes, C.; Palmero, M.; Bellot, J. L.; Castillo, M.; Orts, A.
CORPORATE SOURCE: Department of Interuniversitary Optics, University of Alicante, Alicante, Spain
SOURCE: International Journal of Environmental Studies (2000), 58(1), 67-74
CODEN: IJEVAW; ISSN: 0020-7233
PUBLISHER: Gordon & Breach Science Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This work studied the regulation of lipopolysaccharide-stimulated PGE2 synthesis by traditional nonsteroidal anti-inflammatory drugs (piroxicam and diclofenac) and a selective cyclooxygenase-2 (COX-2) inhibitor (NS-398) in cultured bovine corneal endothelial cells and retinal pigment epithelial cells. The IC50 values of piroxicam and diclofenac were compared with those of NS-398; diclofenac, in both types of cells, had higher potency than piroxicam. Diclofenac seemed to be a COX-2 inhibitor because its IC50 values were similar to those of NS-398. This in vitro cell assay system may be useful for identifying compds. that selectively inhibit COX-2 in ocular tissues.
IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(identification of selective cyclooxygenase-2 inhibitors for eye tissues)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



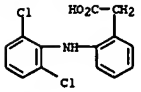
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 15 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:116804 CA
TITLE: Diclofenac and NS-398, a selective cyclooxygenase-2 inhibitor, decrease agonist-induced contractions of the pig isolated ureter
AUTHOR(S): Mastrangelo, Dominique; Wisard, Marc; Rohner, Stephane; Leisinger, Hansjurg; Iselin, Christophe E.
CORPORATE SOURCE: Clinique d'Urologie, Divisions d'Investigations Chirurgicales, Centre Medical Universitaire, Geneva, 1211/4, Switz.
SOURCE: Urological Research (2000), 28(6), 376-382
CODEN: URLRA5; ISSN: 0300-5623
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Non-steroidal anti-inflammatory drugs (NSAIDs) are currently considered a first-line treatment of renal colic. Their action has been ascribed to the inhibition of renal prostaglandin synthesis, which decreases renal blood flow and diuresis, and consequently lowers the pressure in the renal pelvis and ureter. However, the effects of NSAIDs on induced contractions of ureteral smooth muscle have received little attention. Also, there is a lack of clin. relevant spasmolytic drugs for the ureter. Therefore, the authors studied the influence of the non-selective cyclooxygenase (COX) inhibitor diclofenac, a NSAID drug customarily used in the treatment of renal colic, and of NS-398, a selective COX-2 inhibitor, on induced contractions of the pig ureter. Serotonin (0.1-30 μM), norepinephrine (0.1-30 μM) and neurokinin A (0.03-10 μM) induced reproducible concentration-dependent contractions, which were inhibited by diclofenac and NS-398 (10-300 μM) in a concentration-dependent manner. The sensitivity of neurokinin A-induced contractions to diclofenac was 3-4 times greater than that of the amines. Depending on the concentration, inhibition ranged between 25 and 96% of the initially induced contractile activity. In the presence of inhibitors, supramaximal concns. of agonists were unable to trigger recuperation of the initially induced contractions. Prostaglandin F2α did not reverse the effect of diclofenac on agonist-induced contractions. Removal of diclofenac or NS-398 from the organ baths showed that the inhibition was totally reversible. Thus, the non-selective COX inhibitor diclofenac and the selective COX-2 inhibitor NS-398 are almost equipotent in reducing agonist-induced contractions in the isolated porcine ureter. Although the clin. relevance of this spasmolytic effect remains to be demonstrated, the data suggest that patients suffering from renal colic may benefit not only from the anti-diuretic and analgesic effects of diclofenac, but also from its potential spasmolytic properties. Moreover, selective COX-2 inhibitors may have clin. potential, as they may cause fewer side effects.

IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diclofenac and NS-398 decrease agonist-induced contractions of pig isolated ureter in relation to treatment of renal colic)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

L8 ANSWER 15 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

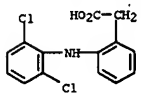
L8 ANSWER 16 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:81971 CA
TITLE: Formulations of adenosine A1 agonists
INVENTOR(S): Bountra, Charanjit; Clayton, Nicholas Maughan; Naylor, Alan
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001045683	A2	20010628	WO 2000-GB4883	20001219 <--
WO 2001045683	A3	20020314		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1239879	A2	20020918	EP 2000-985627	20001219
EP 1239879	B1	20040225		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003519104	T2	20030617	JP 2001-546422	20001219
AT 260119	E	20040315	AT 2000-985627	20001219
US 2003004128	A1	20030102	US 2002-168195	20020618
PRIORITY APPLN. INFO.:			GB 1999-30075 A	19991220
			WO 2000-GB4883 W	20001219

AB A method of treating conditions associated with pain and alleviating the symptoms associated with it comprises administering to a mammal an adenosine A1 agonist or a salt or solvate and an NSAID, e.g., a COX-2 inhibitor. The present invention also provides pharmaceutical formulations and patient packs comprising the combinations. Thus, (2S,3S,4R,5R)-2-(5-tert-butyl-[1,3,4]oxadiazol-2-yl)-5-[6-(4-chloro-2-fluorophenylamino)purin-9-yl]tetrahydrofuran-3,4-diol (I) was prepared in a series of steps by the reaction of (3aS,4S,6R,6aR)-6-(6-chloropurin-9-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxole-4-carboxylic acid with 2,2-dimethylpropionic acid hydrazide followed by the cyclization of the resulting compound, and subsequent treatment with 4-chloro-2-fluoroaniline and deprotection. I and 2-(4-ethoxy-phenyl)-3-(4-methanesulfonylphenyl)pyrazolo[1,5-b]pyridazine (COX-2 inhibitor), were administered at 1% to rats. The compds. showed inhibition of carrageenan-induced edema and allodynia.

IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(formulations of adenosine A1 agonists)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

L8 ANSWER 16 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)

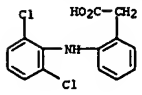


L8 ANSWER 17 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:56086 CA
TITLE: Cyclooxygenase 2 inhibitor-HMG-CoA reductase inhibitor combination for treating neurodegenerative diseases, especially Alzheimer's disease
INVENTOR(S): Waldstreicher, Joanne
PATENT ASSIGNEE(S): Merck & Co. Inc., USA
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001045698	A1	20010628	WO 2000-US34069	20001218 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002115689	A1	20020822	US 2000-731963	20001207

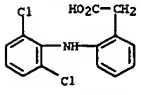
PRIORITY APPLN. INFO.: US 1999-172926P P 19991221
AB The invention provides a drug combination comprised of an HMG-CoA reductase inhibitor and a selective COX-2 inhibitor, which is useful for treating, preventing, delaying the onset of and/or reducing the risk of developing Alzheimer's disease. One object of the invention is to administer the above-described combination therapy to people who do not yet show clin. signs of Alzheimer's disease, but who are at risk of developing Alzheimer's disease. These individuals may already show signs of mild cognitive impairment. Toward this end, the invention provides methods for preventing or reducing the risk of developing Alzheimer's by administering the above-described combination therapy to the at risk persons. Such treatment may halt or reduce the rate of further cognitive decline or, in fact, reverse cognitive decline. The invention also provides a method for preventing cognitive impairment or dementia, reducing the risk of cognitive decline or impairment or reducing cognitive decline or impairment resulting from stroke, stroke, cerebral ischemia or demyelinating disorders.
IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase 2 inhibitor-HMG-CoA reductase inhibitor combination for treating neurodegenerative diseases, especially Alzheimer's disease)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

L8 ANSWER 17 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

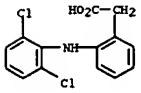
L8 ANSWER 18 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:55728 CA
TITLE: Inhibition of COX in ocular tissues: an in vitro model to identify selective COX-2 inhibitors
AUTHOR(S): Garcia-Cabanes, C.; Palmero, M.; Bellot, J. L.; Castillo, M.; Orts, A.
CORPORATE SOURCE: Department of Interuniversitary Optics, University of Alicante, Alicante, Spain
SOURCE: Journal of Ocular Pharmacology and Therapeutics (2001), 17(1), 67-74
CODEN: JOPTFU; ISSN: 1080-7683
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The aim of this work was to study the regulation of LPS-stimulated PGE2 synthesis by traditional NSAIDs (piroxicam and diclofenac) and a selective COX-2 inhibitor (NS-398), in cultured bovine corneal endothelial cells and retinal pigmentary epithelial cells. The IC50 values of piroxicam and diclofenac were compared with IC50 values of NS-398; diclofenac, in both types of cells, showed higher potency than piroxicam. Diclofenac seemed to be a COX-2 inhibitor because its IC50 values were similar to the IC50 values of NS-398. We suggest that this in vitro cell assay system could be useful for identifying compds. that selectively inhibit COX-2 in ocular tissues.
IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vitro model to identify selective COX-2 inhibitors)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 19 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 135:280 CA
TITLE: Gastrointestinal tolerability of the selective cyclooxygenase-2 (COX-2) inhibitor rofecoxib compared with nonselective COX-1 and COX-2 inhibitors in osteoarthritis
AUTHOR(S): Watson, Douglas J.; Harper, Sean E.; Zhao, Peng-Liang; Quan, Hui; Bolognese, James A.; Simon, Thomas J.
CORPORATE SOURCE: Merck Research Laboratories, West Point, PA, USA
SOURCE: Archives of Internal Medicine (2000), 160(19), 2998-3003
CODEN: AIMDAP; ISSN: 0003-9926
PUBLISHER: American Medical Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Most nonsteroidal anti-inflammatory drugs (NSAIDs) are nonselective cyclooxygenase (COX-1 and CON-2) inhibitors and are associated with a variety of upper gastrointestinal (GI) tract symptoms. The roles of COX-1 and COX-2 in the pathogenesis of these symptoms are unclear. To test whether COX-2 inhibition with rofecoxib would have greater GI tolerability than nonselective COX-1 and COX-2 inhibition, we compared the incidences of (1) treatment discontinuations for GI adverse events (AEs) and (2) prespecified dyspeptic-type GI AEs among patients with osteoarthritis treated with rofecoxib vs. NSAIDs. A prespecified, combined anal. of investigator-reported GI AEs in all 8 double-blind, randomized, phase 2b/3 osteoarthritis trials of rofecoxib was conducted. Patients included men and women with osteoarthritis (N = 5435); there was no upper age limit for entry. Treatments tested included rofecoxib, 12.5, 25, or 50 mg (combined), vs. ibuprofen, diclofenac, or nabumetone (combined). Primary outcomes were the time (by survival anal.) to (1) treatment discontinuation due to GI AEs and (2) first reported dyspeptic-type GI AE. Between-treatment comparisons were made by log-rank test. The number of treatment discontinuations caused by GI AEs during 12 mo was significantly lower (P=.02) with rofecoxib vs. NSAIDs (8.2 vs. 12.0 per 100 patient-years; relative risk, 0.70; 95% confidence interval, 0.52-0.94). The incidence of prespecified dyspeptic-type GI AEs during the first 6 mo was significantly lower (P=.02) with rofecoxib vs. NSAIDs (69.3 vs. 85.2 per 100 patient-years; relative risk, 0.85; 95% confidence interval, 0.74-0.97). However, the difference between treatments in dyspeptic-type GI AEs was attenuated after 6 mo. Rofecoxib was associated with a lower incidence of treatment discontinuations due to GI AEs over 12 mo and a lower incidence of dyspeptic-type GI AEs over 6 mo than treatment with nonselective COX inhibitors, or NSAIDs.
IT 15307-86-5, Diclofenac
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gastrointestinal tolerability of selective cyclooxygenase-2 (COX-2) inhibitor rofecoxib compared with nonselective COX-1, NSAID and COX-2 inhibitors in osteoarthritis)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

L8 ANSWER 19 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 20 OF 56 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 134:348071 CA

TITLE: Role of COX-2 inhibition on the formation and healing of gastric ulcers induced by indomethacin in the rat

AUTHOR(S): Godessart, Nuria; Salcedo, Carolina; Fernandez, Andres G.; Palacios, Jose M.

CORPORATE SOURCE: Research Center, Almirall Prodesfarma, Barcelona, 08024, Spain

SOURCE: Advances in Experimental Medicine and Biology (1999), 469(Eicosanoids and Other Bioactive Lipids in Cancer, Inflammation, and Radiation Injury, 4), 157-163
CODEN: AEMBAP; ISSN: 0065-2598

PUBLISHER: Kluwer Academic/Plenum Publishers

DOCUMENT TYPE: Journal

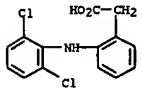
LANGUAGE: English

AB A study was conducted to examine the effect of a selective cyclooxygenase-2 (COX-2) inhibitor on the formation and healing of gastric ulcers induced by a single administration of indomethacin in the rat. Other non-steroidal antiinflammatory agents (NSAIDs) such as diclofenac, ketorolac and aspirin have also been tested. Results suggest that COX-2 is not involved in the development of gastric ulcers induced by NSAIDs. Healing of these ulcers is not affected by treatment with a COX-2 selective inhibitor at doses that it impairs healing in other ulcer models, probably indicating that in different models, different repair mechanisms are involved. Findings do not exclude a role for COX-2 in ulcer healing but they strongly indicate that a functional COX-1 is needed for the repair process to occur.

IT 15307-86-5, Diclofenac
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(role of COX-2 inhibition on formation and healing of gastric ulcers induced by indomethacin in the rat)

RN 15307-86-5 CA

CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 21 OF 56 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 134:261047 CA

TITLE: Etoricoxib (MK-0663): preclinical profile and comparison with other agents that selectively inhibit cyclooxygenase-2

AUTHOR(S): Riendeau, D.; Percival, M. D.; Brideau, C.; Charleson, S.; Dube, D.; Ethier, D.; Falgueyret, J.-P.; Friesen, R. W.; Gordon, R.; Greig, G.; Guay, J.; Mancini, J.; Ouellet, M.; Wong, E.; Xu, L.; Boyce, S.; Visco, D.; Girard, Y.; Prasit, P.; Zamboni, R.; Rodger, I. W.; Gresser, M.; Ford-Hutchinson, A. W.; Young, R. N.; Chan, C.-C.

CORPORATE SOURCE: Departments of Pharmacology, Biochemistry, Merck Frosst Centre for Therapeutic Research, Kirkland, QC, Can.

SOURCE: Journal of Pharmacology and Experimental Therapeutics (2001), 296(2), 558-566
CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

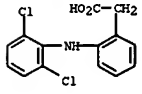
AB We report here the preclin. profile of etoricoxib (MK-0663) [5-chloro-2-(6-methylpyridin-3-yl)-3-(4-methylsulfonylphenyl)pyridine], a novel orally active agent that selectively inhibits cyclooxygenase-2 (COX-2), that has been developed for high selectivity in vitro using whole blood assays and sensitive COX-1 enzyme assays at low substrate concentration Etoricoxib selectively inhibited COX-2 in human whole blood assays in vitro, with an IC50 value of 1.1±0.1 μM for COX-2 (LPS-induced prostaglandin E2 synthesis), compared with an IC50 value of 116±8 μM for COX-1 (serum thromboxane B2 generation after clotting of the blood). Using the ratio of IC50 values (COX-1/COX-2), the selectivity ratio for the inhibition of COX-2 by etoricoxib in the human whole blood assay was 106, compared with values of 35, 30, 7.6, 7.3, 2.4, and 2.0 for rofecoxib, valdecoxib, celecoxib, nimesulide, etodolac, and meloxicam, resp. Etoricoxib did not inhibit platelet or human recombinant COX-1 under most assay conditions (IC50 > 100 μM). In a highly sensitive assay for COX-1 with U937 microsomes where the arachidonic acid concentration was lowered to 0.1 μM, IC50 values of 12, 2, 0.25, and 0.05 μM were obtained for etoricoxib, rofecoxib, valdecoxib, and celecoxib, resp. These differences in potency were in agreement with the dissociation consts. (Ki) for binding to COX-1 as estimated from an assay based on the ability of the compds. to delay the time-dependent inhibition by indomethacin. Etoricoxib was a potent inhibitor in models of carrageenan-induced paw edema (ID50 = 0.64 mg/kg), carrageenan-induced paw hyperalgesia (ID50 = 0.34 mg/kg), LPS-induced pyresis (ID50 = 0.88 mg/kg), and adjuvant-induced arthritis (ID50 = 0.6 mg/kg/day) in rats, without effects on gastrointestinal permeability up to a dose of 200 mg/kg/day for 10 days. In squirrel monkeys, etoricoxib reversed LPS-induced pyresis by 81% within 2 h of administration at a dose of 3 mg/kg and showed no effect in a fecal 51Cr excretion model of gastropathy at 100 mg/kg/day for 5 days, in contrast to lower doses of diclofenac or naproxen. In summary, etoricoxib represents a novel agent that selectively inhibits COX -2 with 106-fold selectivity in human whole blood assays in vitro and with the lowest potency of inhibition of COX-1 compared with other reported selective agents.

IT 15307-86-5, Diclofenac
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

L8 ANSWER 21 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)
(preclin. profile of etoricoxib and comparison with other agents that selectively inhibit cyclooxygenase-2)

RN 15307-86-5 CA

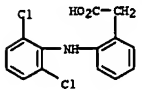
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 22 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 134:172806 CA
TITLE: Gastrointestinal toxicity with celecoxib vs nonsteroidal anti-inflammatory drugs for osteoarthritis and rheumatoid arthritis. The CLASS study: a randomized controlled trial
AUTHOR(S): Silverstein, Fred E.; Faich, Gerald; Goldstein, Jay L.; Simon, Lee S.; Pincus, Theodore; Whelton, Andrew; Makuch, Robert; Eisen, Glenn; Agrawal, Naurang M.; Stenson, William F.; Burr, Aimee M.; Zhao, William W.; Kent, Jeffrey D.; Lefkowith, James B.; Verburg, Kenneth M.; Geis, G. Steven
CORPORATE SOURCE: Dep. of Med., Univ. of Washington, USA
SOURCE: JAMA, the Journal of the American Medical Association (2000), 284(10), 1247-1255
CODEN: JAMAAP; ISSN: 0098-7484
PUBLISHER: American Medical Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Context Conventional nonsteroidal anti-inflammatory drugs (NSAIDs) are associated with a spectrum of toxic effects, notably gastrointestinal (GI) effects, because of inhibition of cyclooxygenase (COX)-1. Whether COX-2-specific inhibitors are associated with fewer clin. GI toxic effects is unknown. Objective: To determine whether celecoxib, a COX-2-specific inhibitor, is associated with a lower incidence of significant upper GI toxic effects and other adverse effects compared with conventional NSAIDs. Design: The celecoxib Long-term Arthritis Safety Study (CLASS), a double-blind, randomized controlled trial conducted from Sept. 1998 to Mar. 2000. Setting: Three hundred eighty-six clin. sites in the United States and Canada. Participants: A total of 8059 patients (≥ 18 yr old) with osteoarthritis (OA) or rheumatoid arthritis (RA) were enrolled in the study, and 7968 received at least 1 dose of study drug. A total of 4573 patients (57%) received treatment for 6 mo. Interventions: Patients were randomly assigned to receive celecoxib, 400 mg twice per day (2 and 4 times the maximum RA and OA dosages, resp.; n=3987); ibuprofen, 800 mg 3 times per day (n=1985); or diclofenac, 75 mg twice per day (n=1996). Aspirin use for cardiovascular prophylaxis (≤325 mg/d) was permitted. Main Outcome Measures: Incidence of prospectively defined symptomatic upper GI ulcers and ulcer complications (bleeding, perforation, and obstruction) and other adverse effects during the 6-mo treatment period. Results: For all patients, the annualized incidence rates of upper GI ulcer complications alone and combined with symptomatic ulcers for celecoxib vs. NSAIDs were 0.76% vs 1.45% (P=.09) and 2.08% vs. 3.54% (P=.02), resp. For patients not taking aspirin, the annualized incidence rates of upper GI ulcer complications alone and combined with symptomatic ulcers for celecoxib vs. NSAIDs were 0.44% vs 1.27% (P=.04) and 1.40% vs. 2.91% (P=.02). For patients taking aspirin, the annualized incidence rates of upper GI ulcer complications alone and combined with symptomatic ulcers for celecoxib vs. NSAIDs were 2.01% vs. 2.12% (P=.92) and 4.70% vs. 6.00% (P=.49). Fewer celecoxib-treated patients than NSAID-treated patients experienced chronic GI blood loss, GI intolerance, hepatotoxicity, or renal toxicity. No difference was noted in the incidence of cardiovascular events between celecoxib and NSAIDs, irresp. of aspirin use. Conclusions: In this study, celecoxib, at dosages greater than those indicated clin., was associated with a lower incidence of symptomatic ulcers and ulcer complications combined, as well as other

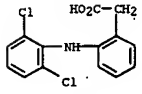
L8 ANSWER 22 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)
clin. important toxic effects, compared with NSAIDs at std. dosages. The decrease in upper GI toxicity was strongest among patients not taking aspirin concomitantly.
IT 15307-86-5, Diclofenac
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gastrointestinal toxicity with celecoxib vs.nonsteroidal anti-inflammatory drugs for osteoarthritis and rheumatoid arthritis in humans.)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 23 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 134:51152 CA
TITLE: Reduced risk of upper gastrointestinal ulcer complications with celecoxib, a novel COX-2 inhibitor
AUTHOR(S): Goldstein, Jay L.; Silverstein, Fred E.; Agrawal, Naurang M.; Hubbard, Richard C.; Kaiser, June; Maurath, Clement J.; Verburg, Kenneth M.; Geis, G. Steven
CORPORATE SOURCE: Section of Digestive and Liver Diseases College of Medicine, University of Illinois at Chicago, Chicago, IL, USA
SOURCE: American Journal of Gastroenterology (2000), 95(7), 1681-1690
CODEN: AJGAAR; ISSN: 0002-9270
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The aim of this study was to assess the rate of upper gastrointestinal (UGI) ulcer complications (bleeding, perforation, or gastric outlet obstruction) associated with celecoxib, a specific COX-2 inhibitor, compared with the rate associated with nonspecific, nonsteroidal anti-inflammatory drugs (NSAIDs). A pooled anal. was conducted of 14 multicenter, double-blind, randomized, controlled trials (RCTs) and a sep. anal. of one long-term open label trial that assessed the efficacy and safety of celecoxib for symptomatic treatment of arthritis. The RCTs enrolled 11,008 patients with osteoarthritis or rheumatoid arthritis treated for 2-24 wk; the long-term open label trial enrolled 5,155 patients receiving celecoxib for a maximum of 2 yr. In the RCTs, patients were randomly assigned to receive placebo (n = 1,864; 208 patient-years), celecoxib 25-400 mg b.i.d. (n = 6,376; 1,020 patient-years), or a comparator NSAID (n = 2,768; 535 patient-years); NSAIDs were (naproxen 500 mg b.i.d., diclofenac 50 or 75 mg b.i.d., or ibuprofen 800 mg t.i.d.). In the long-term, open-label trial, patients received celecoxib 100-400 mg b.i.d. for up to 2 yr (n = 5,155; 5,002 patient-years). The principal outcome measure of this anal. was development of a UGI ulcer complication, which was prospectively defined as bleeding, perforation, or gastric outlet obstruction. Ulcer complications were assessed and adjudicated by persons blinded to the patient's treatment assignment or the study in which the patient participated. In the RCTs, UGI ulcer complications occurred in no placebo patients (0 of 1,864 patients), in 2 of 6,376 celecoxib patients (0.03%), and in 9 of 2,768 patients receiving an NSAID (0.33%), corresponding to annual incidences of 0.20% for celecoxib (p > 0.05 vs placebo) and 1.68% for NSAIDs (p = 0.002 vs celecoxib and placebo). In the long-term open-label trial, nine UGI ulcer complications occurred, for an incidence of 0.17% and an annualized incidence of 0.18%. The incidence of UGI ulcer complications associated with celecoxib was 8-fold lower than with nonspecific NSAIDs. The incidence of ulcer complications observed in celecoxib-treated patients was similar to that in patients receiving placebo in the RCTs, and to that in non-NSAID users reported in the literature.
IT 15307-86-5, Diclofenac
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reduced risk of upper gastrointestinal ulcer complications with celecoxib, a novel COX-2 inhibitor)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

L8 ANSWER 23 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)



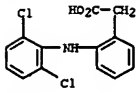
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 24 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 134:36790 CA
TITLE: Inhibition of l-leucine methyl ester mediated killing of THP-1, a human monocytic cell line, by a new anti-inflammatory drug, T614
AUTHOR(S): Sawada, T.; Hashimoto, S.; Tohma, S.; Nishioka, Y.; Nagai, T.; Sato, T.; Ito, K.; Inoue, T.; Iwata, M.; Yamamoto, K.
CORPORATE SOURCE: Department of Allergy and Rheumatology, University of Tokyo School of Medicine, Tokyo, 113, Japan
SOURCE: Immunopharmacology (2000), 49(3), 285-294
CODEN: IMMUDP; ISSN: 0162-3109
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB T614 (3-formylamino-7-methylsulfonylamino-6-phenoxy-4H-1-benzopyran-4-one) is a member of the family of methanesulfonanilide non-steroidal anti-inflammatory drugs (mNSAIDs), most of which act as cyclooxygenase (COX)-2 inhibitors. L-Leucine Me ester (Leu-OME) is a reagent which has been shown to kill phagocytes following interaction with intracellular proteases. There are two pathways whereby Leu-OME becomes cytotoxic to phagocytes. Within lysosomes, Leu-OME is converted into free Leu, which causes disruption of the lysosomes and subsequent cell necrosis. The other is the conversion of Leu-OME into (Leu-Leu)n-OME, which is associated with the induction of apoptosis. In the present study, we examined the action of T614 on Leu-OME mediated killing of THP-1, a human monocytic cell line. We revealed that T614 and phenylmethyl sulfonyl fluoride (PMSF), a serine protease inhibitor, inhibited Leu-OME mediated killing of THP-1 cells. All the other mNSAIDs, including nimesulide (NIM-03), fluosulide (CGP28238), FK3311 and NS398, also rescued THP-1 from Leu-OME-mediated killing, although to a lesser degree. Of the classical NSAIDs tested, a protective effect was observed with diclofenac at high concentration, but not with naproxen or indomethacin. Unlike conventional lysosomal inhibitors, such as chloroquine and ammonium chloride (NH4Cl), T614 and PMSF did not raise lysosomal pH, as measured by flow cytometry using fluorescein isothiocyanate dextran (FITC-dextran). Therefore, the mechanism whereby T614 and PMSF inhibit Leu-OME killing is distinct from that of chloroquine or NH4Cl. Based on the similarity of T614 and PMSF, we suggest that, besides their roles as COX-2 inhibitors, T614 and other mNSAIDs may act as lysosomal protease inhibitors.

IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiinflammatory drug T614 inhibition of L-leucine Me ester-mediated killing of monocyte)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

L8 ANSWER 24 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)

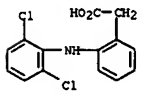


REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 25 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 133:305403 CA
TITLE: Nepafenac, a unique nonsteroidal prodrug with potential utility in the treatment of trauma-induced ocular inflammation: I. Assessment of anti-inflammatory efficacy
AUTHOR(S): Gamache, Daniel A.; Graff, Gustav; Brady, Milton T.; Spellman, Joan M.; Yanni, John M.
CORPORATE SOURCE: Pharmaceutical Products Research, Alcon Research, Ltd., Fort Worth, TX, USA
SOURCE: Inflammation (New York) (2000), 24(4), 357-370
CODEN: INFLD4; ISSN: 0360-3997
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Nepafenac, the amide analog of 2-amino-3-benzoylbenzeneacetic acid (amfenac), was examined in preclin. models for its potential utility as a topical ocular anti-inflammatory agent. Diclofenac was selected as the reference compound In contrast to diclofenac (IC50 = 0.12 μM), nepafenac produced only weak inhibition of cyclooxygenase (COX) 1 (from sheep vesicular glands, in vitro) (IC50 = 64.3 μM). However, amfenac was a potent inhibitor of both COX-1 (IC50 = 0.25 μM) and COX-2 activity (IC50 = 0.15 μM). Ex vivo, a single topical ocular dose of nepafenac (0.1%) inhibited prostaglandin synthesis in the rabbit iris/ciliary body (85-95%) and the retina/choroid (55%). These levels of inhibition were sustained for 6 h in the iris/ciliary body and 4 h in the retina/choroid. Diclofenac (0.1%) suppressed iris/ciliary body prostaglandin synthesis (100%) for only 20 min, with 75% recovery within 6 h following topical administration. Diclofenac's inhibition of prostaglandin synthesis in the retina/choroid was minimal. Nepafenac's inhibitory efficacy and longer duration of action were confirmed in a trauma-induced rabbit model of acute ocular inflammation by monitoring protein or PGE2 accumulation in the aqueous humor. The results warrant further assessment of nepafenac's topical ocular efficacy in the treatment of postoperative ocular pain, inflammation, and posterior segment edema.

IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nepafenac vs. amfenac and diclofenac in the treatment of trauma-induced ocular inflammation)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/724,457

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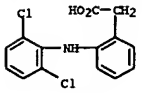
L8 ANSWER 26 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 133:99555 CA
TITLE: Converting COX-inhibiting compounds to derivatives that are selective COX-2 inhibitors as non-steroidal anti-inflammatory drugs
INVENTOR(S): Kalgutkar, Amit S.; Marnett, Lawrence J.
PATENT ASSIGNEE(S): Vanderbilt University, USA
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000040087	A1	20000713	WO 1999-US30219	19991216 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2358241	AA	20000713	CA 1999-2358241	19991216 <--
EP 1148783	A1	20011031	EP 1999-967416	19991216 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9917001	A	20011113	BR 1999-17001	19991216 <--
AU 772705	B2	20040506	AU 2000-23697	19991216 <--
AU 2000023697	A5	20000724		
US 6762182	B1	20040713	US 2001-869384	20010821
PRIORITY APPLN. INFO.:			US 1999-115090P	P 19990107
			WO 1999-US30219	W 19991216

AB A method of altering specificity of cyclooxygenase (COX)-inhibiting non-steroidal anti-inflammatory compds. that have a COOH moiety into an ester or secondary amide analogs specific for COX-2 is presented. The non-steroidal anti-inflammatory drug (NSAID) is selected from the group consisting of fenamic acids, indoles, phenylalkanoic acids, and their pharmaceutically acceptable salts. For example, conversion of free carboxylic acid group in indomethacin to the Me ester afforded the compound which was 132 times more selective as a COX-2 inhibitor than as a COX-1 inhibitor (IC50 (COX -2) .apprx. 0.25 μM; IC50 (COX-1) .apprx. 33 μM). Chain length extension of the Me group in indomethacin Me ester to higher alkyl homologs revealed increases in potency and selectivity against COX -2.
IT 15307-86-5, Diclofenac
RL: RCT (Reactant); RACT (Reactant or reagent)
(conversion of COX-inhibitors into COX-2 selective anti-inflammatory agents)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

L8 ANSWER 26 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)

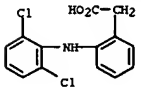


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 27 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 133:99537 CA
TITLE: Amide derivatives for antiangiogenic and/or antitumorigenic use
INVENTOR(S): Kalgutkar, Amit S.; Marnett, Lawrence J.
PATENT ASSIGNEE(S): Vanderbilt University, USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000040088	A1	20000713	WO 1999-US30220	19991216 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6207700	B1	20010327	US 1999-226693	19990107 <--
CA 2358289	AA	20000713	CA 1999-2358289	19991216 <--
BR 9916800	A	20011023	BR 1999-16800	19991216 <--
EP 1146788	A1	20011024	EP 1999-967417	19991216 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002534362	T2	20021015	JP 2000-591862	19991216
AU 760555	B2	20030515	AU 2000-23698	19991216
US 2001034361	A1	20011025	US 2001-818201	20010327 <--
US 6399647	B2	20020604		
PRIORITY APPLN. INFO.:			US 1999-226693	A 19990107
			WO 1999-US30220	W 19991216

AB Secondary amide derivs. of various COOH-containing drugs, such as COOH-containing NSAIDs, for instance, indomethacin were prepared and tested for anti-inflammatory, COX-2 inhibitory, antiangiogenic, and antitumor activity. Many of the tested compds. showed potent activity. Structure activity relations are discussed.
IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(preparation and structure activity relations of amide derivs. of NSAIDs as antiangiogenic and antitumor agents and as inhibitors of cyclooxygenase 2)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

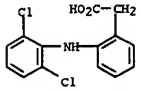


L8 ANSWER 27 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 28 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 133:9109 CA
TITLE: COX-2 inhibitors in combination with NMDA blockers for treating pain
INVENTOR(S): Caruso, Frank S.
PATENT ASSIGNEE(S): Algos Pharmaceutical Corporation, USA
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000029023	A1	20000525	WO 1998-US24317	19981112 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2351224	AA	20000525	CA 1998-2351224	19981112 <--
AU 9914086	A1	20000605	AU 1999-14086	19981112 <--
EP 1146905	A1	20011024	EP 1998-957950	19981112 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002538078	T2	20021112	JP 2000-582069	19981112

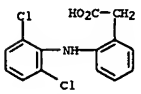
PRIORITY APPLN. INFO.: WO 1998-US24317 W 19981112
AB A method of alleviating a pain state not associated with a cough condition is provided which comprises administering to a mammal exhibiting a pain state not associated with a cough condition a cyclooxygenase-2 inhibitor with a nontoxic NMDA receptor antagonist and/or a nontoxic substance that blocks at least one major intracellular consequence of NMDA receptor activation. An example contains 5-(4-fluorophenyl)-6-[4-(methylsulfonyl)phenyl]spiro[2.4]hept-5-ene as COX-2 inhibitor and dextromethorphan-HBr as NMDA receptor blocker.
IT 15307-86-5, Diclofenac
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(COX-2 inhibitors in combination with NMDA blockers for treating pain)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 28 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)

L8 ANSWER 29 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 133:467 CA
TITLE: Rofecoxib, a specific inhibitor of cyclooxygenase 2, with clinical efficacy comparable with that of diclofenac sodium: results of a one-year, randomized, clinical trial in patients with osteoarthritis of the knee and hip
AUTHOR(S): Cannon, Grant W.; Caldwell, Jacques R.; Holt, Peter; McLean, Barry; Seidenberg, Beth; Bolognese, James; Ehrich, Elliot; Mukhopadhyay, Suarabh; Daniels, Brian
CORPORATE SOURCE: Rofecoxib Phase III Protocol 035 Study Group, Department of Veterans Affairs Medical Center, University of Utah, Salt Lake City, UT, USA
SOURCE: Arthritis & Rheumatism (2000), 43(5), 978-987
CODEN: ARHEAW; ISSN: 0004-3591
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Objective. To compare the clin. efficacy of rofecoxib, a specific inhibitor of cyclooxygenase 2 (COX-2), with that of diclofenac in patients with osteoarthritis (OA) and to evaluate the safety and tolerability of rofecoxib. Methods. We performed a randomized, double-blind, active comparator-controlled trial in 784 adults with OA of the knee or hip. Patients were randomized to 1 of 3 treatment groups: 12.5 mg of rofecoxib once daily, 25 mg of rofecoxib once daily, and 50 mg of diclofenac 3 times daily. Clin. efficacy and safety were evaluated over a 1-yr continuous treatment period. Results. Rofecoxib at dosages of 12.5 and 25 mg demonstrated efficacy that was clin. comparable to that of diclofenac, as assessed by all 3 primary end points according to predefined comparability criteria. Results from secondary end points were consistent with those of the primary end points. There were small statistical differences favoring diclofenac for 2 of the end points. All treatments were well tolerated. Conclusion. Rofecoxib was well tolerated and provided efficacy that was clin. comparable, according to predefined statistical criteria, to that of 150 mg of diclofenac per day in this 1-yr study. Specific inhibition of COX-2 provided therapeutic efficacy in OA.
IT 15307-86-5, Diclofenac
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rofecoxib, a specific inhibitor of cyclooxygenase 2, with clin. efficacy comparable with that of diclofenac sodium in humans with osteoarthritis of knee and hip)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

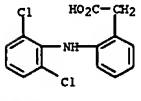


REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 30 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 132:343345 CA
TITLE: Cyclooxygenase 2 (COX-2) inhibitors in combination with centrally acting analgesics for alleviation of pain
INVENTOR(S): Caruso, Frank S.
PATENT ASSIGNEE(S): Algos Pharmaceutical Corporation, USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000029022	A1	20000525	WO 1998-US24045	19981112 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9913988	A1	20000605	AU 1999-13988	19981112 <--

PRIORITY APPLN. INFO.: WO 1998-US24045 A 19981112
AB A method of alleviating a pain state not associated with a cough condition is provided which comprises administering a COX-2 inhibitor and a centrally active analgesic selected from a narcotic analgesic, selected from codeine and hydrocodone; an agonist-antagonist analgesic; and tramadol. A method and analgesic composition therefor is also provided for treating all pain states which comprises administering a COX-2 inhibitor and a centrally acting analgesic selected from a narcotic analgesic other than codeine and hydrocodone; an agonist-antagonist analgesic; and tramadol.
IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase 2 inhibitors in combination with centrally acting analgesics for alleviation of pain)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

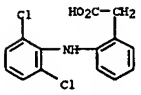
L8 ANSWER 31 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 132:303170 CA
TITLE: Effects of selective and unselective cyclooxygenase inhibitors on prostanoid release from various rat organs
AUTHOR(S): Tegeder, Irmgard; Neupert, Werner; Guhring, Hans; Geisslinger, Gerd
CORPORATE SOURCE: Center of Pharmacology, Johann Wolfgang Goethe-University of Frankfurt, Frankfurt am Main, Germany
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2000), 292(3), 1161-1168
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB It has been assumed that cyclooxygenase-2 (COX-2) is solely responsible for inflammatory processes. Recently, this view has been challenged because COX-2-selective agents caused a delay of gastric ulcer healing and exacerbation of inflammation in rats. To further characterize organ-specific toxic effects of selective and nonselective COX inhibitors, we assessed the eicosanoid release from different rat organs ex vivo after oral administration of the COX -2-selective inhibitor NS-398 and the unselective COX inhibitors diclofenac, meloxicam, and ketorolac. Prostanoid and leukotriene release from tissue fragments of the stomach, kidney, lung, and brain were determined after ex vivo incubation of tissue fragments in Tyrode's solution for 10 min at 37°. Ketorolac (0.1, 0.3, and 0.9 mg/kg) inhibited prostanoid release from all organs most potently and led to a significant increase of leukotriene release from the lung. Effects of diclofenac and meloxicam (1, 3, and 9 mg/kg each) were similar for all organs tested. At 9 mg/kg, 6-keto-prostaglandin F (PGF)1α release from gastric mucosa was reduced by 79.1±11.4 and 87.6±7.7% and PGE2 release from rat kidney was inhibited by 60.4±6.8 and 78.6±16.6% by diclofenac and meloxicam, resp. NS-398 did not reduce prostanoid release from the lung. Consistent with the reported constitutive expression of COX-2, prostanoid release from kidney and brain was reduced by 20 to 30%. The release of 6-keto-PGF1α from gastric mucosa was reduced by 34.7±22.2% at 3 mg/kg and by 86.9±12.7% at 9 mg/kg. At these doses, NS-398 has been previously shown to be COX -2 selective. Because PGF1α is the stable breakdown product of PGI2, these results suggest that COX-2 contributes to PGI2 synthesis in the rat stomach.

IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(effects of selective and unselective cyclooxygenase inhibitors on prostanoid release from various rat organs)

RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

L8 ANSWER 31 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)



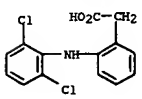
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 32 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 132:87911 CA
TITLE: Celecoxib versus diclofenac in long-term management of rheumatoid arthritis: randomized double-blind comparison
AUTHOR(S): Emery, Paul; Zeidler, Henning; Kvien, Tore K.; Guslandi, Mario; Naudin, Raphael; Stead, Helen; Verburg, Kenneth M.; Isakson, Peter C.; Hubbard, Richard C.; Geis, G. Steven
CORPORATE SOURCE: Department of Rheumatology and Rehabilitation, University of Leeds, Leeds, UK
SOURCE: Lancet (1999), 354(9196), 2106-2111
CODEN: LANCAO; ISSN: 0140-6736
PUBLISHER: Lancet Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: Non-steroidal anti-inflammatory drugs (NSAIDs) inhibit cyclo-oxygenase (COX), which leads to suppression of COX-1-mediated production of gastrointestinal-protective prostaglandins. Gastrointestinal injury is a common outcome. We compared the efficacy, safety, and tolerability of long-term therapy with celecoxib, a COX-1 sparing inhibitor of COX-2, with diclofenac, a non-specific COX inhibitor. Methods: 655 patients with adult-onset rheumatoid arthritis of at least 6 mo' duration were randomly assigned oral celecoxib 200 mg twice daily or diclofenac SR 75 mg twice daily for 24 wk. Anti-inflammatory and analgesic activity and tolerability were assessed at baseline, every 4 wk, and at week 24. We assessed gastrointestinal safety by upper-gastrointestinal endoscopy within 7 days of the last treatment dose at centers where the procedure was available. Anal. was by intention-to-treat. Findings: 430 patients underwent endoscopy (celecoxib n=212, diclofenac n=218). The two drugs were similar in management of rheumatoid arthritis pain and inflammation. Gastroduodenal ulcers were detected endoscopically in 33 (15%) patients treated with diclofenac and in eight (4%) in the celecoxib group (p<0.001). The rate of withdrawal for any gastrointestinal-related adverse event, most commonly abdominal pain, diarrhea, and dyspepsia, was nearly three times higher in the diclofenac-treated group than in the celecoxib group (16 vs. 6%; p<0.001). Interpretation: Celecoxib showed sustained anti-inflammatory and analgesic activity similar to diclofenac, with a lower frequency of upper gastrointestinal ulceration or gastrointestinal adverse events, and tolerability was better.

IT 15307-86-5, Diclofenac
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficacy and safety of celecoxib vs. diclofenac in long-term management of rheumatoid arthritis in humans)

RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 32 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)

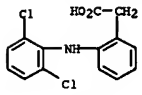
L8 ANSWER 33 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 132:30542 CA
TITLE: Mechanisms of protection afforded by cyclooxygenase inhibitors to endothelial function against ischemic injury in rat isolated hearts
AUTHOR(S): Bouchard, Jean-Francois; Lamontagne, Daniel
CORPORATE SOURCE: Faculty of Pharmacy, University of Montreal, Montreal, QC, H3C 3J7, Can.
SOURCE: Journal of Cardiovascular Pharmacology (1999), 34(5), 755-763
CODEN: JCPCDT; ISSN: 0160-2446
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aim of this study was to assess whether cyclooxygenase (COX) inhibitors protect the endothelial function against the deleterious effect of ischemia and reperfusion. Isolated rat hearts perfused under constant-flow conditions were exposed to 30 min of partial ischemia (flow, 1 mL/min) followed by 20 min of reperfusion, after which coronaries were precontracted with U-46619, and the response to the endothelium-dependent vasodilator, serotonin (5-HT), was compared with that of the endothelium-independent vasodilator, sodium nitroprusside (SNP). In untreated hearts, ischemia diminished selectively 5-HT-induced vasodilation, compared with sham hearts (without ischemia). The vasodilation to SNP was unaffected in all groups. Pretreatment with 6-MNA, 30 μM, a COX-2 inhibitor with some activity on COX 1, diclofenac, 1 μM (COX-1 and -2), or 1-(7-carboxyheptyl) imidazole, 10 μM [thromboxane (TX) synthase inhibitor] but not indomethacin, 10 μM (COX-1 inhibitor) preserved the vasodilation induced by 5-HT after ischemia. Enzyme immunoassays indicated that all COX inhibitors decreased the concentration of TXB2 and 6-keto-PGF1α [stable metabolites of TXA2 and prostacyclin (PGI2), resp.] in coronary effluent during ischemia. Furthermore, indomethacin was the only one to abolish the concentration of PGE2 during ischemia and early reperfusion. No clear trend on ventricular postischemic recovery could be observed between treated and untreated groups under our exptl. protocols. These data suggest that, under our conditions, 6-MNA, diclofenac, and 1-7-CHI, but not indomethacin, protect the endothelial function via a reduction in TX concentration Disparities between COX inhibitors may be due to the complete abolition of PGE2 concentration during ischemia and reperfusion in the indomethacin group.

IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase inhibitors protection of endothelial function in cardiac ischemic injury)

RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

L8 ANSWER 33 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 34 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 131:237687 CA
TITLE: Rofecoxib [Vioxx, MK-0966; 4-(4'-methylsulfonylphenyl)-3-phenyl-2-(5H)-furanone]: a potent and orally active cyclooxygenase-2 inhibitor. Pharmacological and biochemical profiles
AUTHOR(S): Chan, C.-C.; Boyce, S.; Brideau, C.; Charleson, S.; Cromlish, W.; Ethier, D.; Evans, J.; Ford-Hutchinson, A. W.; Forrest, M. J.; Gauthier, J. Y.; Gordon, R.; Gresser, M.; Guay, J.; Kargman, S.; Kennedy, B.; Leblanc, Y.; Leger, S.; Mancini, J.; O'Neill, G. P.; Ouellet, M.; Patrick, D.; Percival, M. D.; Perrier, H.; Prasit, P.; Rodger, I.; Tagari, P.; Therien, M.; Vickers, P.; Visco, D.; Wang, Z.; Webb, J.; Wong, E.; Xu, L-J.; Young, R. N.; Zamboni, R.; Riendeau, D.
CORPORATE SOURCE: Departments of Pharmacology, Biochemistry and Molecular Biology, and Medicinal Chemistry, Merck Frosst Centre for Therapeutic Research, Kirkland, QC, Can.
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1999), 290(2), 551-560
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

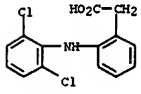
AB The discoveries that cyclooxygenase (COX)-2 is an inducible form of COX involved in inflammation and that COX-1 is the major isoform responsible for the production of prostaglandins (PGs) in the gastrointestinal tract have provided a rationale for the development of specific COX-2 inhibitors as a new class of anti-inflammatory agents with improved gastrointestinal tolerability. In the present study, the preclin. pharmacol. and biochem. profiles of rofecoxib [Vioxx, also known as MK-0966, 4-(4'-methylsulfonylphenyl)-3-phenyl-2-(5H)-furanone], an orally active COX-2 inhibitor, are described. Rofecoxib is a potent inhibitor of the COX-2-dependent production of PGE2 in human osteosarcoma cells (IC50 = 26 ± 10 nM) and Chinese hamster ovary cells expressing human COX-2 (IC50 = 18 ± 7 nM) with a 1000-fold selectivity for the inhibition of COX-2 compared with the inhibition of COX-1 activity (IC50 > 50 μM in U937 cells and IC50 > 15 μM in Chinese hamster ovary cells expressing human COX-1). Rofecoxib is a time-dependent inhibitor of purified human recombinant COX-2 (IC50 = 0.34 μM) but caused inhibition of purified human COX-1 in a non-time-dependent manner that could only be observed at a very low substrate concentration (IC50 = 26 μM at 0.1 μM arachidonic acid concentration). In an in vitro human whole blood assay, rofecoxib selectively inhibited lipopolysaccharide-induced, COX-2-derived PGE2 synthesis with an IC50 value of 0.53 ± 0.02 μM compared with an IC50 value of 18.8 ± 0.9 μM for the inhibition of COX-1-derived thromboxane B2 synthesis after blood coagulation. Using the ratio of the COX-1 IC50 values over the COX-2 IC50 values in the human whole blood assay, selectivity ratios for the inhibition of COX-2 of 36, 6.6, 2, 3, and 0.4 were obtained for rofecoxib, celecoxib, meloxicam, diclofenac, and indomethacin, resp. In several in vivo rodent models, rofecoxib is a potent inhibitor of carrageenan-induced paw edema (ID50 = 1.5 mg/kg), carrageenan-induced paw hyperalgesia (ID50 = 1.0 mg/kg), lipopolysaccharide-induced pyresis (ID50 = 0.24 mg/kg), and

L8 ANSWER 34 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)

AB adjuvant-induced arthritis (ID50 = 0.74 mg/kg/day). Rofecoxib also has a protective effect on adjuvant-induced destruction of cartilage and bone structures in rats. In a 51Cr excretion assay for detection of gastrointestinal integrity in either rats or squirrel monkeys, rofecoxib has no effect at doses up to 200 mg/kg/day for 5 days. Rofecoxib is a novel COX-2 inhibitor with a biochem. and pharmacol. profile clearly distinct from that of current nonsteroidal anti-inflammatory drugs and represents a new therapeutic class of anti-inflammatory agents for the treatment of the symptoms of osteoarthritis and rheumatoid arthritis with improved gastrointestinal tolerability.

IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(potent and orally active cyclooxygenase-2 inhibitor, rofecoxib.)

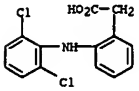
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

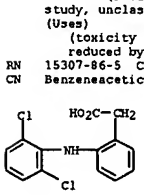
L8 ANSWER 35 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 131:193940 CA
TITLE: Effect of antiinflammatory drugs on COX-1 and COX-2 activity in human articular chondrocytes
AUTHOR(S): Blanco, Francisco J.; Guitian, Ramon; Moreno, Jorge; De Toro, Francisco J.; Galdo, Fausto
CORPORATE SOURCE: Laboratory of Cartilage Research, Rheumatology Unit and Tissue Bank, Juan Canalejo Hospital, Madrid, Spain
SOURCE: Journal of Rheumatology (1999), 26(6), 1366-1373
CODEN: JRHUA9; ISSN: 0315-162X
PUBLISHER: Journal of Rheumatology Publishing Co. Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Objective: To study the effect of steroidal and nonsteroidal antiinflammatory drugs (NSAID) on cyclooxygenase (COX-1 and COX-2) activity in human articular chondrocytes. Chondrocytes were isolated from articular cartilage of donors with no articular disease. Unstimulated and interleukin 1 (IL-1)-stimulated chondrocytes were used as models to study the effects of drugs on COX-1 and COX-2. Cells were incubated with vehicle or drugs; supernatants were removed and the level of prostaglandin E2 (PGE2) in each sample was determined by enzyme immunoassay. IC50 were calculated from the reduction in PGE2 content by different concns. of the test substance by linear regression anal. COX-1 mRNA was detected in unstimulated cells, but stimulation with IL-1 for up 12 h did not modify the levels of COX-1 mRNA. In contrast, COX-2 mRNA was not detectable in unstimulated cells, but it was induced by IL-1. Dexamethasone inhibited COX-2 mRNA expression induced by IL-1. COX-2 protein levels correlated with mRNA expression. Dexamethasone was the strongest drug inhibitor of COX-2 (IC50 = 0.0073 μM). However, it did not inhibit COX-1 activity. Among all NSAID tested, meloxicam and aspirin were the least potent inhibitors of COX-1 (IC50 = 36.6 μM and 3.57 μM, resp.). Indomethacin and diclofenac were the most potent inhibitors of COX-1 (IC50 = 0.063 μM and 0.611 μM, resp.) and COX-2 isoforms (IC50 = 0.48 μM and IC50 = 0.63 μM, resp.). Meloxicam was a more potent inhibitor of COX-2 (IC50 = 4.7 μM) than aspirin (IC50 = 29.3 μM) and similar to piroxicam (IC50 = 4.4 μM). Among all drugs tested dexamethasone showed the greatest selectivity for COX-2 and meloxicam was the NSAID with the best COX-2/COX-1 ratio (r = 0.12). Aspirin and piroxicam were about 8 times more active against COX-1 than COX-2, indomethacin was 7 times more active, and diclofenac was an equipotent inhibitor of COX-1 and COX-2. We found that COX-1 and COX-2 isoforms are expressed in human chondrocytes at rest and in IL-1 stimulated cells, resp. Antiinflammatory drugs have different capacities to inhibit COX enzyme in human articular chondrocytes.
IT 15307-86-5, Diclofenac
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(antiinflammatory drugs effect on COX-1 and COX-2 activity in human articular chondrocytes)
RN 15307-86-5 CA

L8 ANSWER 35 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

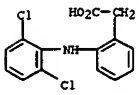
L8 ANSWER 36 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 131:193920 CA
TITLE: Toxicity of human THP-1 monocytic cells towards neuron-like cells is reduced by non-steroidal anti-inflammatory drugs (NSAIDs)
AUTHOR(S): Klegeris, A.; Walker, D. G.; McGeer, P. L.
CORPORATE SOURCE: Kinsmen Laboratory of Neurological Research, University of British Columbia, Vancouver, BC, V6T 1Z3, Can.
SOURCE: Neuropharmacology (1999), 38(7), 1017-1025
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB There is mounting evidence that inflammatory processes, including activation of microglia, are upregulated in Alzheimer's disease. The importance of this phenomenon is indicated by multiple epidemiol. studies showing that patients taking non-steroidal anti-inflammatory drugs (NSAIDs) have a substantially reduced prevalence of Alzheimer's disease. The pharmacol. actions of anti-inflammatory drugs in brain are still uncertain. As a step towards identifying key pharmacol. targets, we developed a neurotoxicity assay based on the property of supernatant media from stimulated human monocytic THP-1 cells to cause human neuroblastoma cell death. Similar neurotoxicity was observed when postmortem human microglia were substituted for THP-1 cells, establishing the validity of the assay for simulating neurotoxicity in human brain. A combination of lipopolysaccharide and interferon-γ was used to activate the THP-1 cells. NSAIDs were effective in inhibiting neurotoxicity by this assay, while steroidal anti-inflammatories and propentofylline had no effect. The neuroprotective potency of NSAIDs appeared to be unrelated to their selective ability to inhibit cyclooxygenase-1 (COX-1) or cyclooxygenase-2 (COX-2). It is suggested that inhibition of monocyte cytotoxicity might be responsible for the apparent beneficial effects of NSAIDs in Alzheimer's disease.
IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(toxicity of human THP-1 monocytic cells towards neuron-like cells is reduced by NSAIDs)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 37 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 131:179484 CA
TITLE: Comparison of inhibitory effects of meloxicam and diclofenac on human thromboxane biosynthesis after single doses and at steady state
AUTHOR(S): Tegeder, Irmgard; Lotsch, Jorn; Krebs, Sabine; Muth-Selbach, Uta; Brune, Kay; Geisslinger, Gerd
CORPORATE SOURCE: Department of Experimental and Clinical Pharmacology and Toxicology, University Erlangen/Nurnberg, USA
SOURCE: Clinical Pharmacology & Therapeutics (St. Louis) (1999), 65(5), 533-544
CODEN: CLPTAT; ISSN: 0009-9236
PUBLISHER: Mosby, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The extent of human cyclooxygenase-1 (COX-1) inhibition by meloxicam, which has been reported to preferentially inhibit cyclooxygenase-2 (COX-2), was evaluated. The effects of meloxicam were compared with those of diclofenac, a nonselective COX inhibitor. COX-1 inhibition was determined by measuring thromboxane B2 (TXB2)-generation from clotting whole blood ex vivo after single oral doses of 7.5 and 15 mg meloxicam and 75 mg diclofenac and at steady state (15 mg meloxicam daily and 150 mg diclofenac daily). The effect was expressed as percentage inhibition of serum TXB2 generation and was directly related to the serum drug concentration with use of a standard sigmoidal Emax model. In terms of inhibition of TXB2 generation, diclofenac was about 1 order of magnitude more potent than meloxicam, indicated by a diclofenac EC50 (concentration of drug required to cause 50% of maximum effect) that was about 10 times lower than that of meloxicam (EC50 diclofenac single doses: 37.50 ± 29.64; EC50 meloxicam single doses: 677.50 ± 189.08). However, serum concns. of meloxicam after administration of 15 mg were approx. 10-fold higher than those of diclofenac. Therefore there was no statistically significant difference in the area under the effect time curve (P = .115) and the mean effect (P = .424) between meloxicam and diclofenac. The EC50 of both drugs was significantly higher at steady state (diclofenac steady state: 87.07 ± 55.24 ng/mL; meloxicam steady state: 1850.12 ± 829.93 ng/mL) than after a single dose (P < .001). These data show that meloxicam inhibits TXB2 generation at clin. relevant doses, although less potently than diclofenac. These data suggest that the COX-2 preference of meloxicam observed in vitro may not result in clin. advantages when the higher dose of 15 mg is needed. Because of the increase in EC50 at steady state, COX-1 is relatively spared when the lower dose of 7.5 mg is administered.
IT 15307-86-5, Diclofenac
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(comparison of inhibitory effects of meloxicam and diclofenac on human thromboxane biosynthesis after single doses and at steady state)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

L8 ANSWER 37 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)



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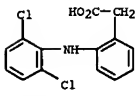
L8 ANSWER 38 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 38 OF 56 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 131:111250 CA
TITLE: Cyclooxygenase-2 inhibition by rofecoxib reverses naturally occurring fever in humans
AUTHOR(S): Schwartz, Jules I.; Chan, Chi-Chung; Mukhopadhyay, Saurabh; McBride, Kathleen J.; Jones, Terry M.; Adcock, Sherilyn; Moritz, Carl; Hedges, Jerris; Grasing, Kenneth; Dobratz, David; Cohen, Robert A.; Davidson, Michael H.; Bachmann, Kenneth A.; Gertz, Barry J.
CORPORATE SOURCE: Merck Research Laboratories, Rahway, NJ, 07065-0914, USA
SOURCE: Clinical Pharmacology & Therapeutics (St. Louis) (1999), 65(6), 653-660
CODEN: CLPTAT; ISSN: 0009-9236
PUBLISHER: Mosby, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cyclooxygenase (COX) exists as constitutive (COX-1) and inducible (COX-2) isoforms. Nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen and diclofenac inhibit both COX-1 and COX-2. The role of COX-2 in the genesis of fever in monkeys and humans was examined with use of the specific COX-2 inhibitor rofecoxib. Rofecoxib was administered to monkeys made febrile by 6 μg/kg i.v. lipopolysaccharide. Induced pyrexia was followed by oral rofecoxib (1 or 3 mg/kg), diclofenac (3 mg/kg), or vehicle. Rofecoxib and diclofenac rapidly reversed the elevated temperature (P <.05 vs. vehicle for 3 mg/kg rofecoxib and diclofenac at 70 to 90 min after dosing). A single-dose, parallel-group, double-blind randomized trial was conducted in 94 patients with fever caused by a viral-type illness. Mean baseline temperature was similar for all groups (.apprx.38.5°). Patients received oral doses of 12.5 mg rofecoxib, 25 mg rofecoxib, 400 mg ibuprofen, or placebo and the mean ± SE change in oral temperature at 4 h after dosing was -0.97° ± 0.11°, -1.19° ± 0.09°, -1.20° ± 0.11°, and 0.01° ± 0.17°, resp. (P <.001 for active treatments vs. placebo). Specific inhibition of COX-2 by rofecoxib results in antipyretic activity in monkeys and humans comparable to dual COX-1/COX-2 inhibitors such as diclofenac or ibuprofen. The data support the hypothesis that it is the COX-2 isoform that is primarily involved in the genesis of fever in humans.

IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 inhibition by rofecoxib reverses naturally occurring fever in humans)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

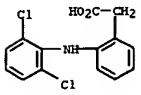
L8 ANSWER 39 OF 56 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 131:111117 CA
TITLE: The analgesic NSAID lornoxicam inhibits cyclooxygenase (COX)-1/-2, inducible nitric oxide synthase (iNOS), and the formation of interleukin (IL)-6 in vitro
AUTHOR(S): Berg, J.; Fellier, H.; Christoph, T.; Grarup, J.; Stimmeder, D.
CORPORATE SOURCE: Department Laboratory Medicine, General Hospital Linz, Linz, A-4020, Austria
SOURCE: Inflammation Research (1999), 48(7), 369-379
CODEN: INREFB; ISSN: 1023-3830
PUBLISHER: Birkhaeuser Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The antiinflammatory effects of lornoxicam in vitro on COX-1/COX-2, NO formation from iNOS, and formation of the pro-inflammatory cytokines TNF-α, IL-1β, IL-6, and IL-8 were investigated. COX-1 inhibition in intact cells was assessed employing 2 systems: measurement of aggregation in human washed platelets and assessment of TXB2 formation in HEL cells. COX-2 inhibition was assessed by measuring 6-keto-PGF, in supernatants of intact cells of LPS-stimulated J774.2 cells (murine) and of Mono Mac 6 cells (human). In whole blood inhibition of COX-1 was performed by measuring TXB2 formation after clotting, and COX-2 inhibition was examined in LPS-stimulated whole blood cultures. The reduction of NO levels as a measure of the inhibition of cellular NO formation was assayed in supernatants of LPS-stimulated RAW 264.7 cells using the Griess reaction. Compound influence on the formation of TNF-α, IL-1β, IL-6, and IL-8 was examined using LPS-stimulated monocytic cells (THP-1) and measurement of cytokine concns. by specific ELISAs. In intact human cells, lornoxicam showed a balanced inhibition of COX-1/-2 exhibiting the lowest IC50 (0.005 μM/0.008 μM) of the large panel of NSAIDs-tested. Similar results were obtained in the whole blood for COX-1/-2. NO formation was dose-dependently inhibited by lornoxicam (IC50 of 65 μM) whereas piroxicam, diclofenac, ibuprofen, ketorolac, and naproxen inhibited the NO formation markedly less. Indomethacin was approx. equipotent with lornoxicam. In stimulated monocytic cells (THP-1), lornoxicam showed a marked inhibition of IL-6 formation (IC50 54 μM) while the formation of TNF-α, IL-1β, and IL-8 was only moderately affected. Of the panel of NSAIDs tested, lornoxicam was found to be the most potent balanced inhibitor of human COX-1/-2. The equipotent COX-isoenzyme inhibition by lornoxicam is complemented by a marked inhibition of IL-6 production and of iNOS-derived NO formation. The in vitro activities described support the marked antiinflammatory and analgesic activities of lornoxicam found in animal models as well as in clin. studies.

IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NSAID effect on COX-1/-2, inducible NO synthase (iNOS), and cytokines)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

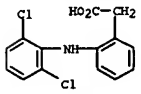
L8 ANSWER 39 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

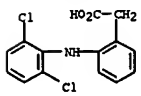
L8 ANSWER 40 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 40 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 131:97193 CA
TITLE: Ex vivo assay to determine the cyclooxygenase selectivity of non-steroidal anti-inflammatory drugs
AUTHOR(S): Giuliano, Francesco; Warner, Timothy D.
CORPORATE SOURCE: Vascular Inflammation, The William Harvey Research Institute, St. Bartholomew's and The Royal School of Medicine and Dentistry, London, EC1M 6BQ, UK
SOURCE: British Journal of Pharmacology (1999), 126(8), 1824-1830
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In this study we describe expts. to establish ex vivo the selectivity of non-steroidal anti-inflammatory drugs (NSAIDs) given in vivo. Anesthetized (Inactin, 120 mg kg-1) male Wistar rats (220-250 g) received an i.v. dose of one of the following compds. (dose mg kg-1): aspirin (20), diclofenac (3), L-745,337 (30), nimesulide (15), salicylate (20), sulindac (10). Blood samples were taken before and up to 6 h after dosing and the plasma obtained from it was tested for its ability to inhibit prostanoid formation in IL-1β-treated A549 cells (COX-2 system) and human washed platelets (COX-1 system). For control the same compds. were also added directly to the assay systems. All drugs, except sodium salicylate, inhibited COX-1 and COX-2 when added directly to the test systems. Plasma from aspirin-treated rats was without effect on either COX-1 or COX-2, consistent with the rapid in vivo metabolism to salicylate. Conversely, plasma from sulindac-treated rats inhibited COX-1 and COX-2 with potencies according with in vivo metabolism to sulindac sulfide. Diclofenac was COX-1/2 non-selective when tested in vitro, but a slightly preferential inhibitor of COX-2 when tested ex vivo. Nimesulide was confirmed as preferential inhibitor of COX-2 both in vitro and ex vivo. L-745,337 was a selective COX-2 inhibitor when tested in vitro or ex vivo. In conclusion, our expts. show clearly (a) NSAIDs inactivation, (b) activation of prodrugs, and (c) NSAIDs selectivity. Our assay provides useful information about the selectivity of NSAIDs that could be extended by the anal. of plasma samples taken from humans similarly treated with test drugs.
IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(ex vivo assay to determine the COX selectivity of NSAIDs)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS

L8 ANSWER 41 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 131:395 CA
TITLE: Induction of an acetaminophen-sensitive cyclooxygenase with reduced sensitivity to nonsteroid antiinflammatory drugs
AUTHOR(S): Simmons, Daniel L.; Botting, Regina M.; Robertson, Philip M.; Madsen, Matthew L.; Vane, John R.
CORPORATE SOURCE: Department of Chemistry and Biochemistry, Brigham Young University, Provo, UT, 84602, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1999), 96(6), 3275-3280
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The transformed monocyte/macrophage cell line J774.2 undergoes apoptosis when treated for 48 h with competitive inhibitors of cyclooxygenase (COX) isoenzymes 1 and 2. Many of these nonsteroid antiinflammatory drugs (NSAIDs), but in particular diclofenac, induce during this time period a COX activity that coincides with a robust induction of COX-2 protein. Induction of this activity requires high, apoptosis-inducing concns. of diclofenac (>100 μM). Prolonged treatment of J774.2 cells with lower doses of diclofenac inhibits COX activity, indicating that diclofenac is a time-dependent, pseudoirreversible inhibitor of COX-2. It is difficult to wash out the inhibition. However, the activity evoked by high concns. of diclofenac has a profoundly distinct COX active site that allows diclofenac, its inducer, to be washed readily from its active site. The diclofenac-induced activity also has the unusual property of being more sensitive to inhibition by acetaminophen (IC50 = 0.1-1.0 mM) than COX-2 induced with bacterial lipopolysaccharide. Moreover, relative to COX-1 or COX-2, diclofenac-induced enzyme activity shows significantly reduced sensitivity to inhibition by diclofenac or other competitively acting nonsteroid antiinflammatory drugs (NSAIDs) and the enzyme activity is insensitive to aspirin. If the robust induction of COX-2 observed is responsible for diclofenac-induced COX enzyme activity, it is clear that COX-2 can, therefore, exist in two catalytically active states. A luciferase reporter-construct that contains part of the COX-2 structure and binds into the membrane showed that chronic diclofenac treatment of fibroblasts results in marked mobilization of the fusion protein. Such a mobilization could result in enzymically distinct COX-2 populations in response to chronic diclofenac treatment.
IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(induction of acetaminophen-sensitive cyclooxygenase with reduced sensitivity to NSAIDs)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



L8 ANSWER 41 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

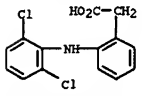
L8 ANSWER 42 OF 56 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 130:231826 CA
TITLE: Development of an in vitro test system for the evaluation of cyclooxygenase-2 inhibitors
AUTHOR(S): Laufer, S.; Zechmeister, P.; Klein, T.
CORPORATE SOURCE: Dep. Drug Research, Merckle G.m.b.H., Blaubeuren, D-89135, Germany
SOURCE: Inflammation Research (1999), 48(3), 133-138
CODEN: INREFB; ISSN: 1023-3830
PUBLISHER: Birkhaeuser Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aim of our study was to establish an in-vitro test system, capable of fast and efficient screening of cyclooxygenase-2 (COX-2) inhibitors. Mononuclear cells were isolated out of human whole blood, in a one-step centrifugation procedure. The time- and concentration-dependent induction of COX-2 expression in the blood monocytes (1 + 106 cells/mL) was evaluated by a kinetic profile. The optimal test conditions were fixed at an LPS concentration of 10 μg/mL and a 5 h incubation time. The test compds. (10-5 to 10-8 mol/L) were set at t = 0 into the assay and were co-incubated for the whole period of COX-2 expression (5 h). The following are representative examples of inhibitors with different distinct selectivity for COX-1/2. Indomethacin as a COX-1 selective compound inhibited PGHS-1 (IC50: 0.002 μM) 200 times stronger than PGHS-2 (IC50: 0,43 μM). Diclofenac had an almost equipotent efficacy on PGHS-1 (IC50: 0.05 μM) and PGHS-2 (IC50: 0.03 μM). NS-398 inhibited highly selective COX-2 (IC50 PGHS-1: 10.75 μM vs. IC50 PGHS-2: 0.16 μM). The model reached the set targets with regard to the differentiation of COX-2 selective compds., the reproducibility of results and practicability of the assay. In contrast to previous propounded theories, we could demonstrate, that mononuclear cells are not unusually sensitive to NSAIDs and apparently possess no further COX isoforms.

IT 15307-86-5, Diclofenac
RL: ANT (Analyte); ANST (Analytical study)
(development of an in vitro test system for the evaluation of cyclooxygenase-2 inhibitors)

RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 43 OF 56 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 130:209502 CA
TITLE: Preparation of 5-alkyl-2-arylaminophenylacetic acids as COX-2 cyclooxygenase inhibitors
INVENTOR(S): Fujimoto, Roger Aki; Mcquire, Leslie Wighton; Mugrage, Benjamin Biro; Van Duzer, John Henry; Xu, Daqiang
PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis-Erfindungen Verwaltungs-Gesellschaft m.b.H.
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9911605	A1	19990311	WO 1998-EP5414	19980826 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6291523	B1	20010918	US 1998-139254	19980825 <--
CA 2298033	AA	19990311	CA 1998-2298033	19980826 <--
AU 9895340	A1	19990322	AU 1998-95340	19980826 <--
AU 743371	B2	20020124		
EP 1007505	A1	20000614	EP 1998-948872	19980826 <--
EP 1007505	B1	20030416		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
TR 200000447	T2	20000721	TR 2000-200000447	19980826 <--
BR 9812010	A	20001212	BR 1998-12010	19980826 <--
JP 2001514244	T2	20010911	JP 2000-508646	19980826 <--
NZ 502669	A	20020201	NZ 1998-502669	19980826
RU 2186762	C2	20020810	RU 2000-107121	19980826
AT 237580	E	20030515	AT 1998-948872	19980826
PT 1007505	T	20030829	PT 1998-948872	19980826
ES 2197508	T3	20040101	ES 1998-948872	19980826
SK 283773	B6	20040108	SK 2000-247	19980826
ZA 9807785	A	19990301	ZA 1998-7785	19980827 <--
MX 200001585	A	20001020	MX 2000-1585	20000215 <--
NO 2000000943	A	20000225	NO 2000-943	20000225 <--
US 6310099	B1	20011030	US 2000-722767	20001127 <--
HK 1031374	A1	20041224	HK 2001-102175	20010326
US 2002013369	A1	20020131	US 2001-950957	20010913
US 6451858	B2	20020917		
US 2002183391	A1	20021205	US 2002-201336	20020723
US 6727281	B2	20040427		
US 2004122254	A1	20040624	US 2003-728244	20031204

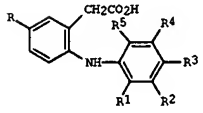
PRIORITY APPLN. INFO.:

US 1997-57803P	P	19970828
US 1997-69837P	P	19971208
US 1998-139254	A1	19980825
WO 1998-EP5414	W	19980826
US 2000-722767	A1	20001127
US 2001-950957	A1	20010913
US 2002-201336	A1	20020723

OTHER SOURCE(S): MARPAT 130:209502

L8 ANSWER 43 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)

GI

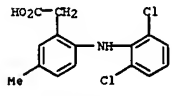


I

AB The title compds. I [R = Me, Et; R1 = chloro, fluoro; R2 = hydrogen, fluoro; R3 = hydrogen, fluoro, chloro, Me, Et, methoxy, ethoxy, hydroxy; R4 = hydrogen, fluoro; R5 = chloro, fluoro, trifluoromethyl, methyl], selective COX-2 cyclooxygenase inhibitors, were prepared IC50 values for I in the COX-2 inhibition assay are as low as 0.005 μM, whereas IC50 values in the COX-1 inhibition assay are > 30 μM. E.g., 5-methyl-2-(2,4-dichloro-6-trifluoromethylanilino)phenylacetic acid was prepared

IT 220991-17-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of alkyl(arylamino)phenylacetic acids as COX-2 cyclooxygenase inhibitors)

RN 220991-17-3 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-5-methyl- (9CI) (CA INDEX NAME)



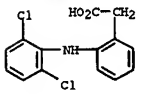
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 44 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 130:75954 CA
TITLE: Cyclooxygenase selectivity and the risk of gastrointestinal complications of various non-steroidal anti-inflammatory drugs. A clinical consideration
AUTHOR(S): Kawai, S.
CORPORATE SOURCE: Institute Medical Science, School Medicine, St. Marianna University, Kawasaki, 216, Japan
SOURCE: Inflammation Research (1998), 47(Suppl.2), S102-S106
CODEN: INREFB; ISSN: 1023-3830
PUBLISHER: Birkhaeuser Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Severe gastro-intestinal complications are a major cause of NSAID-induced deaths in cases of rheumatoid arthritis. The authors measured COX selectivity by an intact cell assay system, and found that NS-398 is a highly COX-2-selective inhibitor. Meloxicam, etodolac, and diclofenac also showed high COX-2 selectivity. Zaltoprofen, loxoprofen-SRS (active metabolite of loxoprofen), 6-MNA (active metabolite of nabumetone), and ibuprofen showed intermediate COX-2 selectivity. The lowest COX-2 selectivities, which means the highest COX-1 selectivities, were observed in indomethacin, aspirin, and oxaprozin. There appears to be a good relationship between our data and some clin. data of severe gastro-intestinal toxicity. The more a given NSAID is selective for COX-2, the safer it is for clin. use. In conclusion, to anticipate the safety of NSAIDs, the authors find that an intact cell assay system, using human cells for measurement of COX selectivity, may be more useful than using direct enzyme assay systems. Following the lecture a discussion ic included.

IT 15307-86-5, Diclofenac
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(cyclooxygenase selectivity determined by a human intact cell system and gastrointestinal complications of nonsteroidal anti-inflammatory drugs)

RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

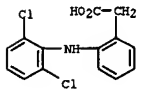
L8 ANSWER 45 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 130:75932 CA
TITLE: Gastrointestinal tolerability of meloxicam compared to diclofenac in osteoarthritis patients.
AUTHOR(S): Hawkey, C.; Kahan, A.; Steinbruck, K.; Alegre, C.; Baumelou, E.; Begaud, B.; Dequeker, J.; Isomaki, H.; Littlejohn, G.; Mau, J.; Papazoglou, S.
CORPORATE SOURCE: Queen's Medical Centre, University Hospital, Nottingham, NG7 2UH, UK
SOURCE: British Journal of Rheumatology (1998), 37(9), 937-945
CODEN: BJRHDF; ISSN: 0263-7103
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Although widely used, non-steroidal anti-inflammatory drugs (NSAIDs) are associated with a high incidence of gastrointestinal (GI) side-effects. Inhibition of the cyclooxygenase (COX) enzyme is the basis for both the efficacy and toxicity of NSAIDs. The discovery of two COX isoforms, constitutive COX-1 and inducible COX-2, has led to the hypothesis that selective inhibition of COX-2 will minimize the potential for GI toxicity without compromising efficacy. The Meloxicam Large-scale International Study Safety Assessment (MELISSA) trial reported here was therefore set up to investigate the tolerability of meloxicam, a preferential inhibitor of COX-2, compared to diclofenac. MELISSA was a large-scale, double-blind, randomized, international, prospective trial, conducted over 28 days in patients with symptomatic osteoarthritis. Patients received either meloxicam 7.5 mg or diclofenac 100 mg slow release, the recommended doses for the treatment of osteoarthritis. Evaluation of the profile of adverse events was the main aim of the trial, together with assessment of efficacy. A total of 9323 patients received treatment (4635 and 4688 in the meloxicam and diclofenac groups, resp.). Significantly fewer adverse events were reported by patients receiving meloxicam. This was attributable to fewer GI adverse events (13%) compared to diclofenac (19%; $P < 0.001$). Of the most common GI adverse events, there was significantly less dyspepsia ($P < 0.001$), nausea and vomiting ($P < 0.05$), abdominal pain ($P < 0.001$) and diarrhea ($P < 0.001$) with meloxicam compared to diclofenac. Five patients on meloxicam experienced a perforation, ulcer or bleed vs seven on diclofenac (not significant). No endoscopically verified ulcer complication was detected in the meloxicam group compared to four with diclofenac. There were five patient days of hospitalization in patients on meloxicam compared to 121 with diclofenac. Adverse events caused withdrawal from the study in 254 patients receiving meloxicam (5.48%) compared to 373 (7.96%) on diclofenac ($P < 0.001$). These differences were attributable to differences in reported GI adverse events (3.02% on meloxicam vs 6.14% on diclofenac; $P < 0.001$). Differences in efficacy, as assessed by visual analog scales, consistently favored diclofenac. In all instances, 95% confidence intervals did not cross zero, suggesting a statistically significant effect. However, differences were small (4.5-9.0% difference) and did not reach pre-determined levels of clin. significance. Nevertheless, significantly more patients discontinued meloxicam because of lack of efficacy (80 out of 4635 vs 49 out of 4688; $P < 0.01$). The MELISSA trial confirms earlier studies suggesting that meloxicam has a significantly improved GI tolerability profile in comparison with other NSAIDs, including diclofenac. These results may in part reflect the preferential COX-2

L8 ANSWER 45 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)
selectivity of meloxicam, although the dose and other aspects of tolerability may be important. These results may provide support for the hypothesis that selective inhibition of COX-2 relative to COX-1 might be an effective approach towards improved NSAID therapy.

IT 15307-86-5, Diclofenac
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gastrointestinal tolerability of meloxicam compared to diclofenac in osteoarthritis patients.)

RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 46 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 130:10645 CA
TITLE: Cox-2 inhibitors in combination with NMDA blockers for treating pain
INVENTOR(S): Caruso, Frank S.
PATENT ASSIGNEE(S): Algos Pharmaceutical Corp., USA
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

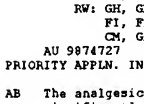
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9850075	A1	19981112	WO 1998-US9252	19980506 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9874727	A1	19981127	AU 1998-74727	19980506 <--

PRIORITY APPLN. INFO.: US 1997-45914P P 19970507
WO 1998-US9252 W 19980506

AB The analgesic effectiveness of a cyclooxygenase-2 inhibitor is significantly enhanced by administering a cyclooxygenase-2 inhibitor with a nontoxic NMDA receptor antagonist and/or a nontoxic substance that blocks at least one major intracellular consequence of NMDA receptor activation.

IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cox-2 inhibitors in combination with NMDA blockers for treating pain)

RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

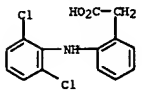


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 47 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 130:10625 CA
TITLE: COX-2-selective carprofen and related compounds for treating pain and inflammation in dogs
INVENTOR(S): Lundy, Kristin Marie; Ricketts, Anthony Paul
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

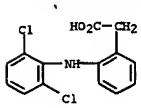
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9850033	A1	19981112	WO 1998-IB662	19980501 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
TW 590773	B	20040611	TW 1998-87106689	19980430
CA 2288759	AA	19981112	CA 1998-2288759	19980501 <--
AU 9869321	A1	19981127	AU 1998-69321	19980501 <--
EP 988034	A1	20000329	EP 1998-915041	19980501 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
BR 9808720	A	20000711	BR 1998-8720	19980501 <--
JP 2000513020	T2	20001003	JP 1998-547869	19980501 <--
NZ 500183	A	20020426	NZ 1998-500183	19980501
NZ 516914	A	20030829	NZ 1998-516914	19980501
ZA 9803722	A	19991104	ZA 1998-3722	19980504 <--
MX 9910148	A	20000228	MX 1999-10148	19991104 <--
AU 773615	B2	20040527	AU 2002-38232	20020508
AU 2002038232	A5	20020620		
US 2003212123	A1	20031113	US 2003-422220	20030424
PRIORITY APPLN. INFO.:			US 1997-45635P	P 19970505
			NZ 1998-500183	A1 19980501
			WO 1998-IB662	W 19980501
			US 1999-308955	A3 19990527

OTHER SOURCE(S): MARPAT 130:10625
AB The invention relates to treating or preventing inflammatory processes and diseases in dogs associated with the activity of inducible cyclooxygenase-2 (COX-2), while at the same time reducing or eliminating undesirable side effects associated with simultaneous inhibition of the activity of constitutive cyclooxygenase-1 (COX-1) by selectively inhibiting COX-2 activity with reference to COX-1 activity, wherein the selectivity ratio or COX-2:COX-1 activity inhibition is at least 3:1 based on ex vivo inhibition levels measured in whole blood. The inhibitor is a member selected from the group of antiinflammatory compds. consisting essentially of salicylic acid derivs., p-aminophenol derivs., indole and indene acetic acids, heteroaryl acetic acids, arylpropionic acids, anthranilic acids, enolic acids, and alkanones; the inhibitor in particular is comprised of the (+)(S)-enantiomer of 6-chloro-α-methyl-9H-carbazole-2-acetic acid.
IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(COX-2-selective carprofen and related compds. for treating pain and inflammation in dogs, and comparative inhibition of COX-1 and -2 by carprofen and other NSAIDs)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

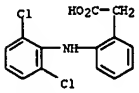
L8 ANSWER 48 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 129:342616 CA
TITLE: Interactions between inducible isoforms of nitric oxide synthase and cyclo-oxygenase in vivo: investigations using the selective inhibitors, 1400W and celecoxib
AUTHOR(S): Hamilton, Lorna C.; Warner, Timothy D.
CORPORATE SOURCE: Vascular Inflammation, The William Harvey Research Institute, St. Bartholomew's and the Royal London School of Medicine and Dentistry, London, EC1M 6BQ, UK
SOURCE: British Journal of Pharmacology (1998), 125(2), 335-340
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Exposure of tissues to endotoxin (LPS) and/or cytokines leads to the induction of both inducible nitric oxide synthase (iNOS) and cyclo-oxygenase-2 (COX-2). It has previously been reported that there is "cross-talk" between these two systems. However, such previous studies have been limited by the availability of highly selective inhibitors. Here we have investigated the interactions between iNOS and COX-2 in vivo using 1400W, an iNOS-selective inhibitor, and celecoxib, a COX-2-selective inhibitor. Infusion of LPS to rats for 6 h caused a time-dependent increase in the plasma concns. of 6 keto-prostaglandin F1α (6 keto-PGF1α and nitrite/nitrate (NO2/NO3), consistent with the induction of iNOS and COX-2. Bolus injection of arachidonic acid (AA) at t = 6 h resulted in a further increase of circulating levels of 6 keto-PGF1α in LPS-treated animals. Treatment of rats with 1400W or the non-selective NOS inhibitor NG-monomethyl-L-arginine (L-NMMA) inhibited the increase in plasma NO2/NO3 but were both without effect on the plasma concentration of 6 keto-PGF1α before or after AA. Treatment with the nonsteroidal anti-inflammatory drugs (NSAIDs), A771726 or diclofenac, or with celecoxib significantly reduced the increase in circulating 6 keto-PGF1α caused by LPS, and the large increase in 6 keto-PGF1α following injection of AA. None of the COX inhibitors affected the increase in plasma NO2/NO3. Dexamethasone, however, significantly inhibited both the increase in 6 keto-PGF1α and the increase in NO2/NO3. In conclusion, the use of selective inhibitors does not support the concept of cross talk in vivo between iNOS and COX-2.
IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(interactions between inducible isoforms of nitric oxide synthase and cyclo-oxygenase in vivo: effects of 1400W and celecoxib)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

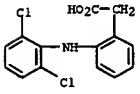
L8 ANSWER 48 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)

L8 ANSWER 49 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 129:62788 CA
TITLE: Differential effect of selective cyclooxygenase-2 (COX-2) inhibitor NS 398 and diclofenac on formalin-induced nociception in the rat
AUTHOR(S): Euchenhofer, Christian; Maihofner, Christian; Brune, Kay; Tegeder, Irmgard; Geisslinger, Gerd
CORPORATE SOURCE: Department of Experimental and Clinical Pharmacology and Toxicology, University of Erlangen-Nurnberg, Erlangen, D-91054, Germany
SOURCE: Neuroscience Letters (1998), 248(1), 25-28
CODEN: NELED5; ISSN: 0304-3940
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Prostaglandins (PGs) are known to be involved in inflammatory and nociceptive processing. Since the discovery of at least two isoenzymes of cyclooxygenase (COX), inhibition of COX-2 has been suggested to be responsible for the therapeutic effects of non-steroidal anti-inflammatory drugs (NSAIDs). In the present study, the effects of a rather selective COX-2 inhibitor, NS-398 (0.3-27 mg/kg i.p.), were studied using the rat formalin test as a model of acute nociception. Diclofenac (non-selective COX inhibitor; 0.3-27 mg/kg i.p.) was used as a control. NS-398 revealed antinociceptive activity only at a dose (27 mg/kg) which results in plasma concns. which most likely do not selectively inhibit COX-2. By contrast, diclofenac inhibited formalin-induced flinching behavior over the whole dose range tested. Our results suggest that PGs mediating nociception in the formalin test of the rat are most likely produced via the COX-1 as well as COX-2 pathways. Thus, in an acute model of nociception a non-selective COX inhibitor may offer advantages as compared to a selective COX-2 inhibitor.
IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(differential effect of selective cyclooxygenase-2 inhibitor NS 398 and diclofenac on formalin-induced nociception)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



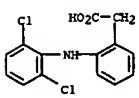
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 50 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 128:149363 CA
TITLE: The effects of a newly developed nonsteroidal anti-inflammatory drug (M-5011) on arachidonic acid metabolism in rheumatoid synovial fibroblasts
AUTHOR(S): Tobetto, Kenji; Yamamoto, Yumiko; Kataoka, Masanori; Ando, Takao; Sugimoto, Kenji; Himeno, Michio
CORPORATE SOURCE: Research and Development Laboratories, Maruho Co., Ltd., Osaka, 531, Japan
SOURCE: Japanese Journal of Pharmacology (1997), 75(4), 371-379
CODEN: JJPAAZ; ISSN: 0021-5198
PUBLISHER: Japanese Pharmacological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB M-5011 (d-2-[4-(3-methyl-2-thienyl)phenyl]propionic acid) is a newly developed nonsteroidal anti-inflammatory drug (NSAID) that displays potent anti-inflammatory and analgesic properties with low ulcerogenic activities in animal models. In this study, the effects of M-5011 on arachidonic acid (AA) metabolism in synovial fibroblasts from patients with rheumatoid arthritis were evaluated and compared with those of other NSAIDs in vitro. Either M-5011 or ketoprofen potently inhibited prostaglandin (PG) E2 production by cyclooxygenase (COX)-2 from exogenous AA in interleukin-1β (IL-1β)-stimulated cells. The IC50 values of M-5011 and ketoprofen were 4.4 + 10-7 and 5.9 + 10-7 M, resp. However, diclofenac and indomethacin were one order less potent. Although the latter two drugs exhibited time-dependent and irreversible inhibition on COX-2 in IL-1β-stimulated cells, the inhibitory effects of M-5011 and ketoprofen were reversible. PGE2 production by COX-1 from exogenous AA in non-stimulated cells was also inhibited by M-5011 with a potency less than that of ketoprofen. In addition, M-5011 inhibited [14C]AA release from prelabeled synovial cells stimulated with bradykinin. However, ketoprofen hardly affected the [14C]AA release. It is likely that the effects of M-5011 on AA metabolism are, in part, responsible for its in vivo efficacy and safety profile.
IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(comparison with; effects of NSAID drug M-5011 on arachidonic acid metabolism in rheumatoid synovial fibroblasts)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 51 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 127:242953 CA
TITLE: Isoenzyme-specific cyclooxygenase inhibitors: a whole cell assay system using the human erythroleukemic cell line HEL and the human monocytic cell line Mono Mac 6
AUTHOR(S): Berg, Jorg; Christoph, Thomas; Widerna, Margot; Bodenteich, Angelika
CORPORATE SOURCE: Department Pharmacology, Topcro Pharma Research GmbH, Linz, Austria
SOURCE: Journal of Pharmacological and Toxicological Methods (1997), 37(4), 179-186
CODEN: JPTMEZ; ISSN: 1056-8719
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB NSAIDs inhibit the conversion of arachidonic acid into Prostaglandin G2 and Prostaglandin H2 which is catalyzed by the enzyme cyclooxygenase (COX). Two genetically distinct isoforms have been discovered, COX-1 and COX-2. While COX-1 is thought to account for homeostatic amts. of eicosanoids, COX-2 is induced during inflammation leading to pathol. amts. of eicosanoids. Since NSAIDs inhibit both COX isoforms, antiinflammatory drug research has refocused to discovering COX-2 inhibitors that do not inhibit COX-1. For this purpose, we have developed a whole cell assay system using the human erythroleukemic cell line HEL as a source for COX-1 and the human monocytic cell line Mono Mac 6 as a source for COX-2. Mono Mac 6 cells express high amts. of COX-2 upon stimulation with lipopolysaccharide (LPS) in the absence of any detectable COX-1 protein. On the other hand, we find HEL cells to naturally express COX-1 protein, but not COX-2. Testing of a panel of NSAIDs as well as some COX-2 specific inhibitors showed that this assay system is suitable for identifying compds. that selectively inhibit either COX-1 or COX -2. This test system offers the advantage of assessing COX-1 and COX-2 inhibitors within the human species, within a similar test set-up, and circumvents the need for tedious purification of either platelets or peripheral blood monocytes.
IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(isoenzyme-specific cyclooxygenase inhibitors: whole cell assay system using human erythroleukemic cell line HEL and human monocytic cell line Mono Mac 6)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

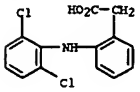


REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

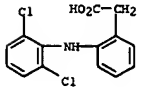
L8 ANSWER 52 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 125:25851 CA
TITLE: Selective inhibition of human cyclooxygenase-2 by meloxicam
AUTHOR(S): Churchill, L.; Graham, A.G.; Shih, C.-K.; Pauletti, D.; Farina, P.R.; Grob, P.M.
CORPORATE SOURCE: Department of Inflammatory Diseases, Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT, USA
SOURCE: Inflammopharmacology (1996), 4(2), 125-135
CODEN: IAOAES; ISSN: 0925-4692
PUBLISHER: Kluwer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human cyclooxygenase-1 (hCOX-1) and -2 were expressed in stable transfected COS A.2 cells and in insect cells using a Sf9 baculovirus expression system. Inhibition of COX activity was examined using both whole cell and microsomal assays. Ibuprofen, naproxen, 6-MNA, diclofenac and indomethacin were selective for hCOX-1 or were equipotent inhibitors for COX-1 and COX-2. Piroxicam was equally inhibitory for both enzymes in the whole cell assay while it preferentially inhibited hCOX-2 in the microsomal assay. However, maximal inhibition of hCOX-2 by piroxicam plateaued at 60%. Nimesulide was equipotent in the whole-cell assay but was five-fold selective for hCOX-2 in the microsomal assay. Meloxicam preferentially inhibited hCOX-2 in the whole cell assay at concns. of 0.01 to 1 μmol/L but was an equipotent inhibitor of both enzymes at higher concns. In the microsomal assay, meloxicam exhibited high selectivity for hCOX-2 (75-fold). The preferential inhibition of hCOX-2 by meloxicam may explain the favorable gastrointestinal profile observed for meloxicam compared with other nonsteroidal antiinflammatory agents.
IT 15307-86-5, Diclofenac
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human cyclooxygenase response to nonsteroidal antiinflammatory agents)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

L8 ANSWER 53 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 124:105962 CA
TITLE: Meloxicam. Part II. In vivo findings
AUTHOR(S): Engelhardt, G.; Boegel, R.; Schnitzler, Chr.; Utzmann, R.
CORPORATE SOURCE: Department Pharmacological Research, Dr. Karl Thomae GMBH, Biberach/Riss, D-88397, Germany
SOURCE: Biochemical Pharmacology (1996), 51(1), 29-38
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Meloxicam is a new nonsteroidal anti-inflammatory drug (NSAID) derived from enolic acid. Preclin. studies have indicated that meloxicam has potent anti-inflammatory activity, together with a good gastrointestinal and renal tolerability profile. This report summarizes studies undertaken to compare meloxicam to other NSAIDs in the inhibition of the inducible cyclooxygenase (COX-2) in inflamed areas (pleurisy of the rat, peritonitis of mice) and their influence on the activity of the constitutive cyclooxygenase (COX-1) in stomach, kidney, brain, and blood. In pleurisy of the rat, meloxicam was twice as potent as tenoxicam, 3 times as potent as flurbiprofen, 8 times as potent as diclofenac, and 20 times as potent as tenidap at inhibiting prostaglandin E2 (PGE2) biosynthesis. In the peritonitis model in mice, meloxicam was approx. twice as active as piroxicam, and more than 10 times as active as diclofenac in the suppression of PGE biosynthesis. Doses of meloxicam sufficient to inhibit PGE2 biosynthesis in the pleural exudate and peritoneal exudate had no influence on leukotriene-B4 (LTB4) or leukotriene-C4 (LTC4) content. The effect of meloxicam on the PGE2 content of rat gastric juice and rat urine was weaker than that of piroxicam or diclofenac. Meloxicam was a weaker inhibitor of the increased PGE2 concentration in brain of rats and mice (induced by convulsant doses of pentetrazole) than piroxicam, diclofenac, or indomethacin. Meloxicam had a weaker effect on serum thromboxane-B2 (TXB2) concentration in rats than piroxicam or tenoxicam. The in vivo findings confirm the results of in vitro tests, conducted sep., showing that meloxicam preferentially inhibits COX-2 over COX-1. COX-2 is the inducible isoenzyme implicated in the inflammatory response, whereas COX-1 has cytoprotective effects in the gastric mucosa. Therefore, a preferential selectivity for one isoenzyme over another, as displayed by meloxicam, may have implications in the clin. setting in terms of a more favorable risk: benefit profile.
IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of meloxicam and other NSAIDs on arachidonic acid metabolism)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

L8 ANSWER 53 OF 56 CA COPYRIGHT 2005 ACS on STN (Continued)



L8 ANSWER 54 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 124:105961 CA
TITLE: Meloxicam: influence on arachidonic acid metabolism. Part. 1. In vitro findings
AUTHOR(S): Engelhardt, G.; Boegel, R.; Schnitzer, Chr.; Utzmann, R.
CORPORATE SOURCE: Department Pharmacological Research, Dr. Karl Thomaae GMBH, Biberach/Riss, D-88397, Germany
SOURCE: Biochemical Pharmacology (1996), 51(1), 21-8
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Meloxicam is a new nonsteroidal anti-inflammatory drug (NSAID) derived from enolic acid. Meloxicam has shown potent anti-inflammatory activity in animal models together with low gastrointestinal and renal toxicity. Studies were undertaken to compare meloxicam to other NSAIDs in their ability to inhibit either constitutive cyclooxygenase (COX-1) or inducible cyclooxygenase (COX-2). COX-1 was isolated as a cell-free enzyme from bovine seminal vesicles or bovine brain or was present in nonstimulated macrophages derived from the guinea-pig peritoneum. COX-2 was induced in peritoneal macrophages stimulated by lipopolysaccharide (LPS) or isolated as a cell-free enzyme from sheep placenta. Of all NSAIDs tested, meloxicam was the most selective inhibitor of COX-2 in intact cells. In cell-free enzyme prepns., however, meloxicam showed the same activity against COX-1 and COX-2. All other NSAIDs tested were more potent inhibitors of COX-1 than of COX-2. The inducible cyclooxygenase COX-2 has been implicated in the mediation of the inflammatory reaction, whereas the products of the constitutive cyclooxygenase COX-1 have cytoprotective effects in the gastric mucosa, support microcirculation in the kidney, and are antithrombogenic. Therefore, differential inhibitory effects of NSAIDs on COX-1 and COX-2 may have a bearing on the risk-benefit profile displayed in clin. practice. Meloxicam shows a preferential inhibitory effect on COX-2 over COX-1, which may be directly related to the favorable tolerability profile with potent anti-inflammatory effects observed in animal studies.
IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(influence of meloxicam and other nonsteroidal anti-inflammatory drugs on arachidonic acid metabolism in relation to constitutive and inducible cyclooxygenase inhibition)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)



L8 ANSWER 55 OF 56 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 123:188000 CA
TITLE: Inhibition of constitutive and inducible cyclooxygenase activity in human platelets and mononuclear cells by NSAIDS and Cox 2 inhibitors
AUTHOR(S): Grossman, C. J.; Wiseman, J.; Lucas, F. S.; Trevethick, M. A.; Birch, P. J.
CORPORATE SOURCE: Molecular Science Department, Glaxo Research and Development, Hertfordshire, SG12 0DP, UK
SOURCE: Inflammation Research (1995), 44(6), 253-7
CODEN: INREFB; ISSN: 1023-3830
PUBLISHER: Birkhaeuser
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A range of NSAIDs (non-steroidal anti-inflammatory drugs) and reported cyclooxygenase (Cox) 2 selective compds. were tested in human freshly isolated platelets and LPS-stimulated mononuclear cells to determine their potency and selectivity as inhibitors of constitutive (presumably Cox 1) and inducible (presumably Cox 2) cyclooxygenase resp. All compds. tested were either equipotent at inhibiting constitutive and inducible cyclooxygenase or were selective for the inducible form. The most selective compound was Dup697 and the least selective, ketoprofen. Several compds. only produced a partial inhibition of constitutive cyclooxygenase as the maximum inhibitor concentration achievable in the assay was limited to 1 mM. With the exception of paracetamol, all compds. were able to produce full inhibition curves against the inducible isoform than in published data for human cloned, microsomal Cox 2. These data suggest that human mononuclear cells are either exquisitely sensitive to some NSAIDs or they may contain another Cox isoform as yet indistinguishable from Cox 2.
IT 15307-86-5, Diclofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of constitutive and inducible cyclooxygenase activity in human platelets and mononuclear cells by non-steroidal anti-inflammatory drugs and cyclooxygenase 2 inhibitors)
RN 15307-86-5 CA
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

L8 ANSWER 56 OF 56 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 120:69065 CA

TITLE: Selectivity of nonsteroidal antiinflammatory drugs as inhibitors of constitutive and inducible cyclooxygenase

AUTHOR(S): Mitchell, Jane A.; Akarasereenont, Pravit; Thiemermann, Christoph; Flower, Roderick J.; Vane, John R.

CORPORATE SOURCE: Med. Coll., St. Bartholomew's Hosp., London, EC1M 6BQ, UK

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1993), 90(24), 11693-7
CODEN: PNASA6; ISSN: 0027-8424

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Constitutive arachidonate cyclooxygenase (COX-1) is present in cells under physiol. conditions, whereas inducible arachidonate cyclooxygenase (COX-2) is induced by some cytokines, mitogens, and endotoxin presumably in pathol. conditions, such as inflammation. Therefore, the authors have assessed the relative inhibitory effects of some nonsteroidal antiinflammatory drugs on the activities of COX-1 (in bovine aortic endothelial cells) and COX-2 (in endotoxin-activated J774.2 macrophages) in intact cells, broken cells, and purified enzyme prepns. (COX-1 in sheep seminal vesicles; COX-2 in sheep placenta). Similar potencies of aspirin, indomethacin, and ibuprofen against the broken cell and purified enzyme prepns. indicated no influence of species. Aspirin, indomethacin, and ibuprofen were more potent inhibitors of COX-1 than COX-2 in all models used. The relative potencies of aspirin and indomethacin varied only slightly between models, although the IC50 values were different. Ibuprofen was more potent as an inhibitor of COX-2 in intact cells than in either broken cells or purified enzymes. Sodium salicylate was a weak inhibitor of both COX isoforms in intact cells and was inactive against COX in either broken cells or purified enzyme prepns. Diclofenac, EW755C, acetaminophen, and naproxen were approx. equipotent inhibitors of COX-1 and COX-2 in intact cells. BF 389, an exptl. drug currently being tested in humans, was the most potent and most selective inhibitor of COX-2 in intact cells. Thus, there are clear pharmacol. differences between the two enzymes. The use of such models of COX-1 and COX-2 activity will lead to the identification of selective inhibitors of COX-2 with presumably less side effects than present therapies. Some inhibitors had higher activity in intact cells than against purified enzymes, suggesting that pure enzyme prepns. may not be predictive of therapeutic action.

IT 15307-86-5, Diclofenac
RL: BIOL (Biological study)
(constitutive and inducible arachidonate cyclooxygenase inhibition by,)

RN 15307-86-5 CA

CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]- (9CI) (CA INDEX NAME)

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